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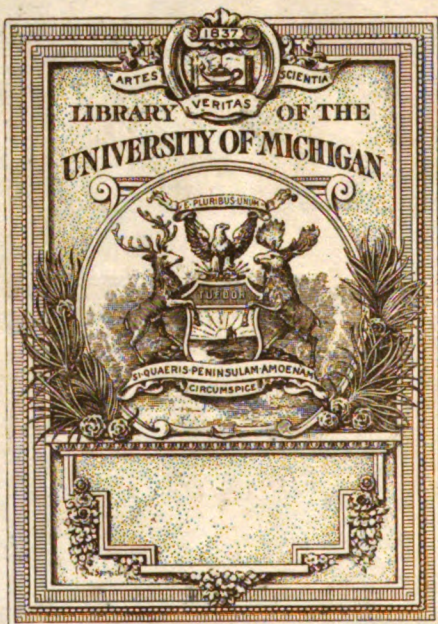
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*Publications from the Laboratories
of the Jefferson Medical College ...*

Jefferson Medical College Hospital



THE GIFT OF
Dr. A. S. Warthin

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1904

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INTRODUCTION.

The accompanying Reprints are of articles written by workers in the Laboratories of the Jefferson Medical College Hospital, or are based on reports or studies made in the institution. Several published articles are not included, among which should especially be mentioned a number of papers by Dr. H. F. Harris, formerly Associate Professor of Pathology in the Jefferson Medical College. Reprints of the writer's studies on Changes in the Myocardium (Proceedings of the Pathological Society of Philadelphia, n.s. Vol. VI) are at present unavailable.

The present volume also includes an index of 2500 reports based on examinations conducted in the Laboratories.

W. M. L. C.

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THE EARLY LESIONS OF ARTERIOSCLEROSIS, WITH SPECIAL REFERENCE TO ALTERATIONS IN THE ELASTICA.*

BY W. M. L. COPLIN, M.D.,

Professor of Pathology in the Jefferson Medical College.

[From the Laboratories of the Jefferson Medical College Hospital.]

The cardiovascular phenomena of arteriosclerosis, of which you ask me to consider the early stages, appear to offer the clinician a picture possessing more definiteness and much sharper outlines or delimitations than the pathologist well can appreciate. The very extensiveness of vascular disease is to the clinician the basis of an essential syndrome, for such I take it to be, containing many and varied lesions. The frequency with which certain changes in the vessels and in the heart, and I might say the nerves and possibly other superficial soft tissues as well as the viscera, are associated leads the clinician to infer that this is all part of a general process. With this view I am not at all prepared to take issue; but pathologists are prone to see some major essential feature which constitutes the basis of even a general condition, and make this change the center about which subsidiary alterations can be more or less definitely grouped.

As an example of this method of classifying, or possibly I had better say correlating, phenomena, let me digress for a moment, to call

*Read before the Pathological Society of Philadelphia, as a part of a Symposium on Arteriosclerosis, Feb. 25, 1904.

your attention to what of course is well known, and therefore better illustrates the point that I am attempting to make. In those lesions associated with inefficient progression at the mitral orifice—whether due to stenosis or regurgitation—we recognize a tendency toward distention of the pulmonary capillaries, fibrosis and pigmentation of the lung, hypertension of the pulmonary artery, alterations in the right ventricle, including the myocardium, valves, and orifices, eventually marked venous distention, red atrophy of the liver, cyanotic kidney, and an impressive list of concomitant but intimately associated structural alterations manifested by, in some instances, characteristic functional disturbances. Here the pathologist, in common with the clinician, recognizes that the essential feature of this long and rather complicated association of processes—many of them dissimilar—can be traced to faulty execution of function primarily restricted to the mitral area. One readily could cite other instances in which wide-spread alterations depend upon some primary, possibly it would be well to say essential, lesion to which other associated abnormalities are subsidiary or at least secondary. Now to apply this somewhat rambling statement to the matter immediately at hand—is it possible for us to recognize in the wide-spread devastation of advanced arteriosclerosis some primary, and therefore necessarily constant, alteration upon which, or rather to which, all other changes are superadded?

Those who are to discuss with us to-night the changes occurring in the kidney, in the alimentary canal, in the central nervous system, and elsewhere, would probably agree that the

primary structural alteration lies somewhere in the cardiovascular system. Apparently alterations in this part of the almost universally diseased organism are necessary to the clinical as well as the pathological concept of the disease under consideration. I think it may safely be predicated that we can look upon the changes in the heart muscle as depending upon alterations in the coronaries or changes in stress, or both, and therefore that the early lesions of arteriosclerosis are not to be sought in any primary change occurring in the myocardium. Such changes may be correlated, and possibly some alterations may precede important structural modifications in the cardiac blood-supply, but still, I take it, the essential alteration must be sought in the arteries themselves. Here we are at once confronted by difficulty in determining exactly what is the constant or more nearly constant change in the vessels. Pathologists see mainly evidence of structural change in the artery, arteriole, capillary, and vein, justifying the terms angiosclerosis used by Thoma¹ and vasculitis with essentially the same meaning adopted by Weichselbaum.²

Before going further let me suggest that the term sclerosis has its limitation, as Gibson³ properly suggests; even Thoma, who is rather an extremist, would not take the ground that the whole of the vascular change is covered by the term sclerosis. Sclerosis in the sense that the vessels are harder, that there is an actually induced induration as an essential part of the process, is true only in part. Vessels may be, in certain stages of the change under consideration, without conspicuous fibrosis or other alteration such as one would ordinarily consider an

important feature of the general picture of so-called arteriosclerosis. Coats and Auld⁴ further urge objection to the term sclerosis as it implies hardening, while ignoring the new formation of tissue that they consider is the fundamental factor in the process. Mott in a way evades and possibly improves this concept by the use of the term degeneration, speaking of cardiovascular degeneration or arterial degeneration, but here the idea of degeneration as it appeals to the pathologist seems to be somewhat different from the picture confronting the clinician. Both are right, but each looks at the shield from a different point of view. The clinician sees degeneration and retrograde change manifested probably by functional inefficiency or inadequacy. The pathologist looks for some structural lesion that falls within a definite catalogue or class, the limitations of which are often arbitrary, sometimes illogical, and they may be impossible to determine with any degree of accuracy.

As a further complication to a clear appreciation of the morbid process under consideration, we are embarrassed by the multitude of alterations, the relation of which, one to another, in the present state of our knowledge, cannot fully be appreciated. Before the appearance of Rokitansky's book (1846) the different stages of atheroma were only confusedly recognized, and not until 1856⁵ did this eminent worker and thinker fully crystallize and unify previously conflicting and discordant views. The morbid anatomist wishes more specific information upon the position, in our scheme, of easily recognized lesions: aneurism, ectasial arteritis, the obliterative arteries of Fried-

lander,⁶ endarteritis proliferans, the thrombosing arteritis of Thoma, the angiosclerosis preferred by Thoma to arteriosclerosis, arteriolitis used by Letulle⁷ and others, the peri- or endarteritis of syphilis, or that type of endarteritis luetica (Heubner), or the hereditary syphilitic arteritis of Barlow;⁸ the periarteritis of Kussmaul and Maier,⁹ and the supra-arterial subepicardial fibroid nodular lesion described by Knox; the so-called spontaneous endarteritis that Camuset¹⁰ thinks is a manifestation of arteriosclerosis, the endarteritis cartilaginosa of Marburg, senile calcification of the arteries, held by Coats and Auld not to be atheromatous, the arterial hypermyotrophy of Savill, the specific degenerative cortical arterial lesions discussed by Berkeley¹¹—where and how we shall correlate all of these, or how many of them enter into the clinical picture of arteriosclerosis, it is impossible at present to say.

Two of the most conspicuous and most constant arterial changes in the condition under consideration are atheroma and the arteriocapillary lesion called by Gull and Sutton¹² a fibrosis, but recognized by a number of other writers as being but part of a change involving arterioles, and called by some writers arteriolitis. Even here authorities are not uniform; Ziegler and Thoma among the pathologists, and most German clinicians, make atheroma and arteriocapillary fibrosis parts of arteriosclerosis. The French just as persistently adhere to the belief that the arteriole change is distinct from that lesion, involving large trunks or relatively large branches, and called by various names, among which the most popular are atheroma, nodular arteritis, and arteritis deformans, as

used by Virchow. Letulle¹³ says chronic arteritis affecting the aorta is atheroma, involving the arterioles it is arteriosclerosis, but we voluntarily confound the two conditions.

The ablest English writers are divided upon the question. Mott apparently includes almost everything under the head of arterial degeneration, making this practically synonymous with arteriosclerosis as used by the German writers. Russell¹⁴ just as consistently, and I think with great force and propriety, insists that atheroma is a distinct form, though it may be coincident with changes involving the arterioles. For the purpose of this discussion the change in the capillaries associated with arteriosclerotic edema and important nutritional disturbances may be excluded, and whatever early changes I may discuss with you can be grouped under the head of arteritis, with the distinct reservation that the inflammatory character of the process is by no means established. It is not necessary to retrace all the views suggesting the inflammatory nature of the affection, although no less an authority than Virchow¹⁵ saw in atheroma changes that he regarded as manifestations of inflammation. The important change, and it seems to me the primary alteration upon which we should focus our inquiry, is the change in the smaller arterial branches, and it is to a study of this lesion that I would particularly invite your attention. Without at all committing ourselves as to its inflammatory nature, which I am rather inclined to disregard, it may be well for us to look for a moment at the causes, or at least such etiologic factors as appear to be in more or less intimate relation with the change in question.

Certain of these causes may be extrinsic or exogenous, arising from without. Among these causes will be classed alcoholism, plumbism, possibly the noxious influences of tobacco, and other preformed poisons, a list of which need not be given. Of the poisons arising within the body should be mentioned those active in intestinal intoxication, which may have something to do with the evolution of arterial disease; the exact nature of the active toxic product is unknown. Whether it is some absorbed bacterial toxin, some normal excretory product of the intestine, some result of proteolytic changes going on in the alimentary canal, some normal or abnormal secretion, remains yet to be determined. The French school strongly urge the influence of alimentary intoxications in the production of arteriosclerosis, and Bergouignan¹⁶ thinks the benefit of a milk diet rests largely upon (1) the admitted diuretic action of milk and (2) its very low toxicity. The view of Huchard and also Runeberg, that endarterial disease is due to a toxin in the blood, while possible, remains unproven. Von Noorden found arteriosclerosis in 155 of 343 diabetics, and Feiner noted the frequent association of the two conditions; Grabe¹⁷ thinks that possibly some cases of diabetes can be attributed to sclerosis of the vessels in the floor of the fourth ventricle.

Gilbert and Lion¹⁸ claim priority¹⁹ in the demonstration that atheroma could be induced by the injection of bacterial toxins. If injection of toxic bodies of a kind normally produced within the intestine can be responsible for arterial lesions, then we should expect to find, in the blood of arteriosclerotic patients,

agglutinating reactions against certain of the intestinal flora. While this problem has been studied it is not yet definitely established that certain members of the intestinal flora yield toxins whose action determines the occurrence of arterial disease. Therese²⁰ has shown that the toxins of bacteria can cause acute arteritis; streptococcus filtrates produce the same vessel changes as unfiltered cultures. Gilbert and Lion state that arterial lesions may be produced through bacterial action in one of three ways: (1) combined trauma of the vessel and infection;²¹ (2) cultures of microbes; (3) toxins.

Undoubtedly an important factor in the production of arteriosclerosis is overwork; this excessive demand thrown upon the circulatory organs may be a response to active brain work such as occurs in professional men, men of affairs, gamblers, and speculators. Hill and Oliver have shown instrumentally that cerebral activity raises the blood-pressure. Excessive vascular demand seems to have much to do with the production of the disease in question. This is shown by the at times almost local occurrence of arterial change; for example, in the arms of blacksmiths, and in all the limbs of overworked horses. Our President²² lays particular stress upon overeating as a cause. This may mean overwork on the part of the digestive and absorptive apparatus, or it may indicate the introduction of foods containing bodies rich in toxic qualities, or possessing a molecular constitution rendering them easily converted into toxic products.

Some of the internal secretions, about which we know so little and speculate so much, undoubtedly possess the capacity to produce

important circulatory disturbances. Clinically, these are recognized when thyroid products in excess enter the circulation and in the highly selective therapeutic action of bodies of adrenal origin. Josue²³ has produced atheroma by the repeated intravenous injection of adrenalin in rabbits, using three drops of a 1-to-1000 solution, given on alternate days, the lesion usually appearing after five or six injections. His results have been corroborated by Gouget.²⁴ The last named observer suggests that possibly arteriosclerosis in all its forms depends either upon direct or indirect action manifested through the adrenal. In a guinea-pig which had received during one month a daily dose of 50 centigrammes of carbonate of lead, there was found at autopsy marked arteriosclerosis and adrenals nearly double the normal size. Sargent²⁵ has shown that there is an infectious suprarenalitis which may give rise to sudden death in an infectious disease—for example, pneumonia. Harbinson²⁶ reports a case of a woman aged 47 years, with bronzing of the skin, showing a distribution characteristic of Addison's disease, and in which also the indications point to arteriole change, as shown by the presence of symptoms of Raynaud's disease, affecting the hands, nose, and ears. Vaquez²⁷ reports a case of persistently high arterial tension which at autopsy showed an adenoma of the adrenal. The same observer suggests that in saturnism there may be an adrenal irritation that is responsible for the change in tension and the tendency to arteriosclerosis. In the discussion Josué referred to his experimental studies and stated that, with Bernard, he was at present studying

the adrenals from cases of atheroma; they have reached the conclusion that in such cases the glands show evidences of increased activity. These scanty observations with regard to the relation between adrenal activity and arteriosclerosis are highly suggestive and demand careful clinical and experimental study and further observation.

In 1901 one of the assistants in the laboratories of the Jefferson Medical College Hospital expressed a desire to study the normal histology and diseases of the adrenals, and for this purpose we collected a large number of these organs. From pressure of other duties the study remains uncompleted. I have gone over sections from some of these and find 22 cases of arteriosclerosis in which sections from one or both adrenals have been prepared. Only five of these are not markedly altered, and in four of the practically normal specimens but one of the pair has been available for study. The change does not seem constant, and the amount of material is inadequate for sweeping conclusions; in 8 there are areas of necrosis, in 5 marked increase in the fibrous tissue, in 3 tuberculosis, and in 1 a secondary neoplasm. In but two instances (sclerosis 1, tuberculosis 1) is the disease bilateral, and in neither of these is it of the same degree in both organs. In one case I have been unable to detect any lesion that could be presumed to have a specific value, although in common with other sections the cells of the medulla are granular, often shrunk from the surrounding reticulum, and but feebly tingible by the usual dyes. As most stain reactions are essentially chemical phenomena, variation must be looked upon as resulting

from some alteration in the chemistry of the affected elements. In the light of Josué's experiments this phase of adrenal action merits most careful inquiry.

There seems little doubt nowadays that the change recognized as an acute arteritis occurring in typhoid, scarlet fever, variola, influenza, and other infectious disease of an acute nature, may constitute the basis upon which the more general arteriosclerosis can be implanted, often not becoming evident until months or possibly years after the infectious process to which it was due has passed away. Bureau²⁸ has described the clinical features of acute inflammation of the aorta. Ford²⁹ has collected eighteen cases of acute arteritis in influenza. Letulle³⁰ thinks the acute arteritis is often preliminary to chronic arteritis, atheroma, arteriosclerosis, and aneurism. Holst³¹ reports an acute aortitis secondary to gonorrhea and arthritis and terminating in aneurism; there was cellular infiltration extending through the media and adventitia, and containing cocci. A similar case is reported by Moore.³² Rabe³³ and other observers state that acute aortitis and proliferating endarteritis may accompany acute rheumatism; the coronaries, and hence the nutrition of the heart, may be affected. He places acute rheumatism among the causes of arteriosclerosis. Hess³⁴ reports two instances of thrombophlebitis complicating acute rheumatism.

Mallory³⁵ described proliferative changes in the endothelium of the vessels in typhoid, and while he made no suggestion that it might constitute an initial stage of inflammation of these structures, one can easily understand the pos-

sibility of such being the case. Thayer³⁶ in his articles discussing arteritis and arterial thrombosis in typhoid has fully considered the arterial lesions that may accompany enteric fever, and the subject is reviewed by Steiner,³⁷ who reports a most instructive case. The reasonable assumption with regard to the thromboses seen in typhoid is that they must depend upon some endovascular lesion; Rolleston³⁸ thinks they are usually bacterial, and Wright³⁹ suggests that the excess of lime salts resulting from a milk diet may be contributory; still the conviction that thrombosis means, in most instances, inflammation involving the intima of the vessels affected may be taken as established, and therefore constitutes an argument in favor of the belief that typhoid often is attended by endovascular alteration which may form the basis of later degenerative change. That other infectious diseases, to varying degrees, attack the integrity of the vascular wall is further supported by the studies of Orłowski,⁴⁰ who collected thirty-six reported instances of thrombosis of the abdominal aorta in infectious disease; Oettinger⁴¹ describes localized arteriosclerosis occurring in the young and due to, or at least following, acute infective disease. Simitzky⁴² has shown that arteriosclerosis has no specific age limitation, and when occurring in youth there is a reasonable basis for the assumption that the acute infectious diseases may indirectly lay a foundation for subsequent sclerotic changes.

The relation of renal disease to arteriosclerosis is too well known to demand any special mention. Syphilis as a factor is admitted, but we are unprepared to adopt the view of Wil-

liams,⁴³ who holds that syphilis is the chief cause of arteriosclerosis as well as aneurism. Whether the arterial changes associated with gout and lithemia depend upon these conditions or upon the causes that give rise to them is not established.

Clinicians are prone to lay great stress upon age as an etiologic factor in the production of arterial disease, but the condition is by no means restricted to the aged. Jacobi⁴⁴ collected twenty-eight cases, and reported one of aneurism in early life. Fenomenoff has reported a congenital aneurism of the aorta. Le Boutil-lier⁴⁵ has collected thirty-three cases of aneurism in persons under 20 years of age. Black⁴⁶ reports a popliteal aneurism in a boy of 10 years. Andral has observed calcifying aortitis in a girl of 5 years. Montard-Martin records an instance of atheroma in the arch of the aorta in a boy about 2 years of age. Berg-hinz⁴⁷ reports an autopsy on an infant of 18 months with arteriosclerotic changes in the heart; typic lesions of syphilis were also present. He refers to another similar case. Adler⁴⁸ states that Young observed sclerotic arterial changes in an infant of 15 months, Meigs in an infant of 5 months, and Seitz found, in 148 cases of arteriosclerosis, seventeen patients who were between 10 and 29 years of age. In the discussion of Adler's paper Brill⁴⁹ referred to a well marked case in a girl of 12 years, verified by autopsy; Brill and Libman⁵⁰ also review arteriosclerosis in early life. Riesman⁵¹ reports universal calcification of the arteries in a boy of 3 years. Hirtz⁵² has seen probably a dozen cases in children. Felatoff⁵³ and Barlow⁵⁴ have described arteritis in the young. Erich-

sen⁵⁵ has observed atheromatous patches in children 3, 5, and 7 years old. Simitzky's observations are referred to above. The writer⁵⁶ has seen instances in childhood, and has recorded a case in which congenital dislocation of the hip in a child dying at the age of 7 was complicated by evident arteriosclerosis. M'Crorie submits data which, in my mind, adequately demonstrate that we have laid too much stress on age, sex, alcohol, and syphilis as causes of atheroma. Many observers have shown that individuals may be very old and show no arterial degeneration. The most advanced age of which I can find any record is the often quoted case of Thomas Parr, who died at the age of 152, and whose arteries were described by Harvey as showing no evidence of degeneration. Broadbent says that in long-lived families arterial tension is low. It is a clinically observed fact that those who live to advanced age commonly possess arteries relatively free from sclerotic change.

Osler suggests the occurrence of tissue inadequacy as a cause of arteriosclerosis. Bruce⁵⁷ under the term "family heart" refers to people whose cardiovascular system is affected by the stress of less than 50 years, and often fails early, sometimes before 30; three to five or more members of the same family may be affected. In some instances of arteriosclerosis heredity seems implicated; Herrick⁵⁸ mentions a family of this kind, and such cases may resemble those falling within the term "family heart" used by Bruce. Adler⁵⁹ thinks hereditary predisposition an important factor. Whether the condition inherited be heightened tension, tissue inadequacy in Osler's sense, or

a proclivity to the excessive production of, or abnormal sensitiveness to, certain poisons, is not known.

Von Manteuffel⁶⁰ has observed, in limbs amputated for frost-bite, the evidences of arteriosclerosis, and has produced the initial lesions of the disease by spraying the legs of rabbits with ether. He thinks the late appearance of gangrene after freezing is due to the slowness with which obliterative lesions develop in the affected vessels.

Allbutt⁶¹ suggests that omitting obliterative arteritis, neuritic arteritis, and periarteritis nodosa, the following classes of arteriosclerosis may be suggested: (1) The involuntary—common in old people, often hereditary, not necessarily or usually associated with rise of arterial pressure; the nature of this form, whether intrinsic or extrinsic, does not lie in high living. This kind, he states, may be vaguely referred to as the "faltering rheums of age." (2) The mechanical—the result of long-persisting high blood-pressure of whatsoever origin. (3) The toxic—due to such causes as lead, alcohol, or syphilis, usually met with in younger persons, in some of whom pressure rises, in others not.

The foregoing does not by any means cover the causes or conditions with which arteriosclerosis may be associated, but with all these varied factors, what seems to be an almost, if not quite, constant feature in them all? At some time or another in the evolution of each there is a marked rise in arterial tension. Gowers,⁶² Moxon,⁶³ Allbutt, and a number of equally discerning observers accept vascular stress, at least in part, as an influential factor

in the production of atheroma. Williams in discussing Broadbent's paper thinks that the high arterial tension of arteriosclerosis in the earlier stages at least is due to an effort at excretion of a poison. All writers on disease of the cardiovascular system lay particular stress upon this heightened blood-pressure; by some it is called by a name indicating exactly what it is—heightened arterial tension. Others have given it a special name. Clifford Allbutt⁶⁴ terms it his "own jade" hyperpiesis. Russell calls it arterial hypertonus.⁶⁵ Savill⁶⁶ includes the change under the head arterial hypermyotrophy.⁶⁷ M'Crorie⁶⁸ thinks mechanical irritation is not the exciting but the chief predisposing cause of atheroma. He thinks it depends on an irritant acting on the fenestrated membrane of Henle by way of the vasa vasorum, but the nature of the irritant is unknown. According to M'Crorie, atheroma always begins in the membrane of Henle adjacent to the media.

Sherrington⁶⁹ believes that the main work of the heart is expended not directly in propelling the blood but in dilating the arteries. This work must be increased as a result of high tension from no matter what cause, and again increased blood-pressure must throw extra strain upon the vessels throughout their course. The recognition of this fact has led to inquiry as to whether this recurring exercise of the muscles presiding over the arteriole can produce hypertrophy of the muscle elements in the wall of the vessels.

Russell⁷⁰ thinks recurring or persisting hypertonus is, under suitable conditions, associated with an increase in the muscle layer.

Grassmann⁷¹ thinks that arteriosclerosis is, in a way, a diffuse neoformation in the vessels with a certain tendency to malignancy; he believes that the process is initially hypertrophic, although later associated with inflammation and degeneration. Gibson⁷² pictures thickened media as an evidence of increased quantity of unstriated muscle in that structure. The usual methods resorted to for determining the relative thickness of the media by comparing it to the total thickness of the wall of the vessel, or to the diameter of the lumen, or estimating the relation between these factors, cannot be trustworthy, as no one can estimate how much contraction has occurred post mortem, and therefore to what degree the thickness of the muscle wall and transverse diameter of the vessel have been influenced. Herringham⁷³ has attempted to overcome the technical difficulties besetting such inquiry by counting the muscle nuclei on longitudinal and transverse section, recognizing that no matter whether the vessel be distended or contracted the number of nuclei should remain the same in the absence of hypertrophy. He could recognize no increase in the muscle coat, and while his method constitutes a distinct advance it is open to objections similar to those already mentioned. Savill⁷⁴ described thickening of the middle layer, which he called arterial hypermyotrophy. While there is a general agreement that the demonstration of hypertrophy in the media is beset with difficulties that cannot at present be overcome, there is equally a unanimity of opinion that sooner or later degenerative changes occur in the media and between that membrane and the intima, often influencing the latter, and

marked by hyaline and fibroid transformation, to which reference will be made later.

The views of Thoma⁷⁵ have been extensively promulgated and very generally accepted. With his students this eminent authority has collected data to establish the correctness of his opinion that the initial change in arteriosclerosis, following the increased tension, is a widening of the arterioles, followed by reduction in the speed of flow, which in turn gives rise to proliferative changes in the intima of the widened artery, bringing about a readjustment of the vascular lumen. I gather from the writings of Thoma and his students that the relaxation of the vessel wall is to be regarded as depending upon what might be termed muscle fatigue incident to the maintenance of continuous tension. While constantly referring to the loss of elasticity in such vessels, primarily he laid no particular stress upon alterations in the elastica, to which I am convinced we should look for some, if not all, of the initial alterations upon which the change in question must depend. If, as is held by Thoma, the proliferation of the intima is in response to a lessened pressure, then we should expect it to be uniform and not excentric as commonly observed. The same response might at this moment be inserted with regard to the belief that the proliferative changes in the intima depend upon the presence of an intravascular irritant. As is well known, vessels showing the earliest stages of the sclerosis commonly manifest it only in a part of the wall. Asymmetry in distribution is one of the most constant features of the changes both early and late, and the signet-ring appearance of sectioned sclerotic vessels is so con-

stantly present as to be almost, if not absolutely, characteristic. I shall return to this point later.

Observations concerning the elastica in diseases of the vessels are by no means restricted to recent contributions to the literature of vessel disease. Practically all observers working with advancing or advanced lesions in the arteries, and many students of experimental pathology, have directed more or less attention to this phase of the subject. Langhans⁷⁶ speaks of indifferently formed elastica in the larger arterial trunks and growth of new elastic tissue in the vessels at the base of the brain; he also describes a cellular infiltration of the elastic lamina with the formation of new fibrous tissue. Baumgarten⁷⁷ considers the changes in elastica seen in chronic arteritis and endarteritis, but with special reference to luetic disease of the brain vessels; he described new-formed elastica and broken residual elastic lamina. Eppinger⁷⁸ maintains that the primary change in the evolution of aneurism is rupture of the elastic elements in the media; Manchot⁷⁹ holds essentially the same view. Thoma⁸⁰ says it is quite clear that arteriosclerosis is dependent upon reduction in the elasticity of vessels, a sort of an angiomalacia, which may be due to functional overdistention, acute and chronic disturbances of metabolism (gout), chronic poisonings (lead, mercury), or specific diseases (typhoid, syphilis). In the later reference he reiterates his views with regard to the relation of widened lumen to proliferative intima, to which I have already referred. Thoma and his school (v. Zwingman,⁸¹ Eberhardt,⁸² Mann⁸³ Waegner⁸⁴) find the lacerated elas-

tica described by Eppinger and Manchot, but suggest the possibility that the change is physiological (!), as it may be found in large and small arteries of adults, in the new-born, and at intermediate ages. Coats and Auld⁸⁶ describe and figure separated elastica, but regard the change as a later manifestation, believing the membrane intact in the earlier stages. According to these writers the media is affected, in atheroma, only when the elastica is altered. In one instance they figure broken elastic lamina under an atheromatous patch and express the conviction that rupture of the membrane of Henle may be followed by inflammatory or reparative changes in the media. Dmitrijeff⁸⁶ concludes that in arteriosclerosis there is both disappearance and new growth of elastic tissue; the former, essentially a degeneration, is seen in the early stages, and primarily is marked by changes in tingibility, followed by morphologic alteration, and eventually necrosis. The newly formed elastica, like some other young tissues, possesses less resistance to noxious influences and hence yields readily before excessive pressure or deleterious bodies. Knox mentions disappearance of the external elastic lamina in the supra-arterial epicardial fibroid nodules that he describes. Boy Teissier and Sesques⁸⁷ refer to changes in the elastic fibers of the coronary branches in the condition they term xerosis of the heart. Malkoff⁸⁸ in his study of the relation of trauma to the formation of aneurism describes many changes in the elastica and details the stages of its regeneration. Abramow⁸⁹ concludes that the elastic tissue seen in the arteries in syphilitic disease of the vascular

system is not newly formed but results from the splitting of the preëxisting elastica of the inner elastic membrane of the vessels. Herringham⁹⁰ looks upon swelling and splitting of the elastica as one of the earliest changes in arteriosclerosis; he thinks regeneration, or at least new formation, occurs. Auld, in the discussion of Herringham's paper, said he had described splitting of the elastica in the arteries of the pia in Bright's disease. Cesaris-Demel⁹¹ describes new formation of elastica in the tunica media of the aorta in aortitis of arteriosclerotic origin. Grohe⁹² states that in true inflammation of the arteries elastic tissue is increased, but not in phlebitis; it is formed from preëxisting elastica. In aneurism there is a reduction in the quantity of elastic tissue, which is fragmented, with curled ends. He observes that the vessels of the brain are especially rich in elastica. Grassmann⁹³ believes the initial important change in arteriosclerosis is loss of elasticity, which implies of necessity some defect in the elastica. Most clinicians recognize inelasticity as an essential factor of the fully developed disease. Matuszewicz⁹⁴ describes calcareous changes in the elastic lamina in arteriosclerosis; such infiltration may be seen in normally placed elastica as well as in newly formed fibers beyond the usual zone. Our knowledge of calcification strongly indicates that it is a regressive process occurring in degenerating or especially necrotic or necrosing fields, and therefore its presence in the architecture of a vessel wall constitutes strong presumptive evidence that some retrograde lesion is in progress. I quite agree with Marburg⁹⁵ that the hyaline change described by many of

the older writers may reasonably be ascribed to change in the elastica; swollen and straightened fibers lose their characteristic stain reaction, and of course suffer morphologic alterations. Sections stained by the ordinary routine methods present changes that one would not hesitate to pronounce degenerative, but proper elastic tissue stains at once correct the misapprehension. As Marburg correctly observes, what appeared hyaline by ordinary technique often so appears when treated for elastica, which may be taken as supporting the view that elastica, as well as fibrous tissue, may be subject to hyaline transformation; intermediate tinctorial reactions also occur.

Jores⁹⁶ in his studies of the elastica describes a fatty metamorphosis of the internal elastic lamina, reacting to Sudan III and also to osmic acid, and also new formation of the elastica in the intima and media of arteriosclerotic vessels. Gilbert and Lion⁹⁷ state that the atheroma experimentally produced in rabbits does not differ from that seen in man; they describe the change as a sclerocalcareous transformation. The calcification begins in the elastic fibers, which lose their property of fixing picric acid, and become vitreous, thick, brittle, and rigid. At the periphery of the nodule such calcific fibers become continuous with or extend beyond and merge into more or less normal fibers of the vessel wall.

Babcock⁹⁸ states that "loss of elastic resistance on the part of a vessel is due to degeneration and atrophy of the elastic fibers of the media, and this destructive change in the middle coat may be due to the long continuance of

excessive blood-pressure or to sudden, frequent alterations of blood-pressure."

In 1900, shortly after the appearance of Weigert's paper,⁹⁹ we began, in the laboratories of the Jefferson Medical College Hospital, a systematic study with special reference to the condition of the elastica in a number of conditions. While much of this work has been done by my assistants—for whose cordial coöperation I here express my indebtedness—it was particularly through the enthusiastic labors of Mr. George V. Ridley, a student of medicine, that it was possible to secure a comparative study of some 1200 sections stained by the usual routine methods, and especially for elastica. Many of these were from cases of recognized arteriosclerosis and associated with characteristic changes. Others were from patients from whom arteriosclerotic alterations were believed to have been absent, and as a rule such belief was corroborated by histologic study. It is quite impossible to review all these cases, as they constitute practically the entire collection of pathologic material accumulated in the laboratory through a number of years. The arteries particularly studied were those situated in the heart, kidney, pancreas, some part of the alimentary canal (stomach or intestine), and lung. In only a small number of instances were arteries from the muscles available for the study. After the investigation was begun other tissues were added.

I shall cite no specific cases, but give only the alterations most frequently observed; even in the earlier changes I think it may constantly be recognized that the elastic tissue of the arterioles, and to a lesser degree of the larger

trunks, shows, in practically all instances, some more or less marked deviation from the normal. Fragmentation, swelling, separation, and curling of the fragmented ends constitute the most common early alteration. An arteriole may show but a single break in the elastica, but the retracted and thickened end of the broken fiber usually will be seen clumped and posed like the head and neck of a serpent about to strike. The immediately adjacent laminæ show irregular contortions, often extending beyond their normal limits, as though, in retraction, they had pulled or recoiled out of place. In the relatively early stages the media external to the elastic layer is the seat of no discernible lesion. Just inside the membrane of Henle there is always more or less alteration (see Fig. 1). This part of the intima is thickened and reticulated, containing a varying number of round or slightly elongated cells, between which the deli-



FIG. 1.—Artery; early stage of arteriosclerosis. Stained especially for the demonstration of the elastica; Weigert's method, followed by Mayer's carmalum and picroindulin. *a*, Broken and curled elastica, which at places shows fragmentation. *b*, Fibrohyaline thickening of the intima; within this stratum can be seen short crinkled fragments of elastica that have been regarded by some authors as efforts at regeneration. Fragmentation of the elastic lamina is particularly marked just above the leader from letter *b*. The media in this vessel appears much broader than normal, but it is most difficult, if not impossible, to say that it is hypertrophied.

cate fibrils of the reticulum are dispersed. In the later stages, within this newly formed fibrous tissue, a varying number of new elastic fibrils can be recognized; as a rule the latter are short, thinner than those in the normal stratum, and less wavy in contour. The source of these new fibers can be conjectured only; the view that they are parts of, or developed from, preëxisting elastica may be possible in some instances, but the situation often must be taken



FIG. 2.—Artery; arteriosclerosis. Stained especially for the demonstration of the elastica; Weigert's method, followed by carmalum and picroindulin. *a*, Fragmented and separated elastica. *b*, Fragmented and curled elastica; note the swelling of the isolated fragment and the curled end at *b*. *c*, Unusually crinkled elastica resulting from yielding and recoil due to solution in continuity at *a* and *b*. *d*, From just below the leader from *d* to upper part of drawing there is no break in the elastica. It will be observed that in that part of the vessel still possessing a practically normal elastica there is no thickening of the intima and subintimal stratum, while the area of altered elastica is overlaid by a fibrohyaline newly-formed tissue containing bits of elastic tissue. There is some fragmentation of the external elastic lamina which is present in this specimen, but absent from the arteries from which Figs. 1 and 3 were made.

as strongly against this view. At what I take to be a later stage (Fig. 2) the dissociation is more marked, and the fibers appear grosser and less regular in their undulating character. The finely fibrillated subendothelial new-formation of fibrous tissue is often more hyaline, and the external elastic lamina, when present, may be the seat of similar changes. The media that in the earlier stage appeared normal or possibly broader than normal now seems thinned, often

irregularly so, and beneath the areas of fragmented or dissociated elastic fibrils a varying degree of mononuclear infiltration usually can be recognized. This condition has been noted by many observers already mentioned, and commonly is interpreted as indicating that the elastica has yielded before the inflammatory

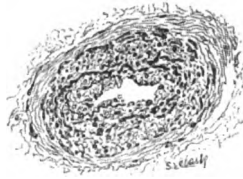


FIG. 3.—Artery; advanced arteriosclerosis. Stained especially for the demonstration of the elastica; Weigert's method, followed by carmalum and picroindulin. In this specimen little more than irregular fragments of the elastic lamina are present. The endothelium no longer form a separate layer, but, as the result of proliferative changes, the inner stratum is composed of young connective tissue cells. There may be some doubt as to whether this vessel during life transmitted blood.

process which, in a sense, has permeated or extended into the middle layer. The muscle layer appears to have given way as the result of extension of the trauma, and the accompanying cell accumulations appeal to me as being essentially reparative in nature. New fibrous tissue is in course of production, and with this there is a varying quantity of evidently young elastica, in some specimens very much more than in others. In the more advanced lesion, as affecting the smaller arteries the dissociation and fragmentation of the elastica with advanced atrophy of the muscle layer are most striking (see Fig. 3). Little of the normal architecture of the vessel remains. The fragments of elastica are but slightly wavy, the irregular separation and distribution most marked, and the whole picture that of dissolu-

tion and almost lawless attempts at restitution rather indiscriminately mixed together.

A point upon which additional information especially is desired is the influence of sudden lengthening of the elastica of vessels. Fragmentation in a circular direction can readily be demonstrated, but longitudinal sections of vessels I have studied in a most inadequate manner. There may be evidence of circular splitting and longitudinal dissociation, as indicated in Fig. 4. If my views are correct such appearance could be due to axial stretching, splitting of the elastic lamina, and the two

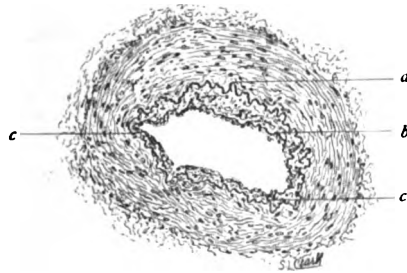


FIG. 4.—Split elastica that may have resulted from longitudinal fissuring. *a*, Outer fragment; *b*, inner fragment; *c*, *c*, points where outer and inner fragments join circumferentially. Between the two strata is the usual hyalofibrous reparative tissue.

fragments slipping upon each other while ends (circumferentially considered) remain intact. If a broad rubber band be laid on the flat one layer upon the other, the two layers can be slid latterly without any great stress on the ends; comparing this crude illustration to a vessel such splitting and sliding would probably result in separation and the intercalation of reparative elements between the two parts of the separated lamina as indicated in the figure.

Between the hurriedly drawn descriptions just given one may recognize myriad kaleido-

scopic pictures of intermediate or allied stages that, to one with my own bias of opinion, appear to be manifestations of a lesion primary in the elastica and characterized by imperfectly evolved efforts at repair. Such efforts are partly in the direction of regeneration of the elastic tissue and, probably to a greater degree, a fibrous substitution for a more highly constituted tissue. The regeneration of elastic tissue is admitted by most writers on the process of repair. Even in vessels its growth has been fully recognized by many observers, although perfect restoration is admittedly difficult. Salvia¹⁰⁰ in his study of vessel anastomosis after resection shows that nearly complete regeneration is possible, all parts being restored except the elastica. The evolution of elastic tissue in other forms of repair has been fully established, and proliferation of elastica in other pathological processes widely studied. New elastic tissue in hepatic cirrhosis has been observed by Melnikow-Rasewedenkow,¹⁰¹ Hohenemser,¹⁰² Jores,¹⁰³ Flexner,¹⁰⁴ Oliver,¹⁰⁵ and others. Its production in tumors has been investigated by Melnikow-Rasewedenkow,¹⁰⁶ Williams,¹⁰⁷ Collina,¹⁰⁸ Abel,¹⁰⁹ Federmann,¹¹⁰ Meinel,¹¹¹ Bindi,¹¹² Zeigler,¹¹³ Hansemann,¹¹³ Hamilton,¹¹⁴ and others, and unpublished studies made by McKinnie in the writer's laboratory are fully confirmatory of the work done by previous investigators. Pearce¹¹⁵ has shown that the elastica is increased in lungs the seat of chronic passive congestion, and attributes to it the increased firmness of the organ. The studies of Pezzolini¹¹⁶ on the regeneration of elastica have not been available. In the earlier stages of its evo-

lution elastica must be extremely susceptible to strain, and hence its repair must be beset with great difficulties; I think clinicians are agreed that marked cases of arteriosclerosis reach stages at which they stand still for long periods. In such instances the retrograde changes must be met by some progressive equivalent competent to oppose the continuous stress of the blood-pressure. I have seen no evidence of muscle restoration, and therefore assume that the elastica meets the demand. Rolleston¹¹⁷ in speaking of the law of parsimony observes that where nature can save the production of such expensive structure as muscle by the evolution of tissue like elastica she may do so. Much more is this likely where the production of muscle must necessarily be fraught with insurmountable difficulty. When we consider the constantly changing volume of vessels there is no cause to wonder at the inadequate, even abortive, effort at elastica production.

Assuming the hypothesis that the initial change in arteriosclerosis is in the elastica the question at once arises, what induces it? Roy and Adami¹¹⁸ have shown that suddenly applied resistance to the onward flow of the blood produces organic changes in the aortic and mitral valves, and edema, sometimes hemorrhages, in the endocardium. Evidently overstrain means tension on the elastica, and overstrain, admittedly a factor in arteriosclerosis, should try to the limit the elastic structures of the vessels. Such excess must be followed by solution in continuity, and this naturally by reparative efforts. Want of adequate nutrition and constant mechanic interference with the process of repair must lead to

degenerative change in the formative tissue, and hence the hyalin and necrotic processes constantly observed in these structures. Could anything but strain similarly influence elastic tissue? This is the day of lytic substances, the specificity of whose action is little short of the miraculous. Among such bodies may be mentioned the hemolysins, nephrolysins, hepatolysins, myolysins, and many others. Eijkman¹¹⁹ has shown that certain bacteria evolve an elastica-dissolving enzyme, and it is not improbable that within our bodies deleterious substances of similar nature may be produced. The assumption that such toxic bodies exist and that their action is as indicated would lead us a step further than Thoma's suggestion of angiomalacia, and give what might be termed elastomalacia a place of primary importance in the evolution of arteriosclerosis. The foregoing hypothesis might lead us to inquire whether the elastic tissues other than those in the vessels ever suffer in arteriosclerosis. Probably this aspect of the question has not been studied, but the fact that Lancereux found emphysema in 34 per cent of his cases of arteriosclerosis and Gull and Sutton note the occurrence of interstitial nephritis in 60 per cent of the cases of emphysema are observations of more than passing interest. Eppinger believes that the elastic tissue is reduced in emphysema, and the studies of Isaaksohn¹²⁰ and also those of Auld¹²¹ and Sudsuki¹²² and others indicate that the elastica is profoundly altered.

I have said next to nothing concerning the very gross and conspicuous lesion commonly termed atheroma, feeling that it is a late stage

of arteriosclerosis, and therefore not within the scope of this paper. But as bearing upon changes in the elastica I should like to call attention especially to that form characterized by the development of grayish-white, wavy, slightly elevated, linear tracings or striæ—mentioned by Moxon over a quarter of a century ago—occurring particularly in the aorta, following the long axis of the affected vessel, and now called linear atheroma.¹²³ I have had an opportunity to study but one instance of this type, and certainly it strikes one as being a reparative change, essentially a scar, possessing most suggestive differences from the ordinary type of atheroma, with which, however, it may be associated. While not tending to discuss arteritis deformans, my conviction is that Hippolyte Martin¹²⁴ is correct in laying stress upon the influence of obliterative disease of the *vàsa vasorum* in its production.

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117. *Brit. Med. Jour.*, vol. ii, 1868, p. 155.
118. *Brit. Med. Jour.*, vol. ii, 1888, pp. 1321 and 1396.
119. *Centralbl. f. Bakt.*, Nov. 5, 1903, p. 1.
120. *Virchow's Arch.*, Bd. liii, p. 466.
121. Selected Researches in Pathology, London, 1901.
122. *Virchow's Arch.*, Bd. 157, H. 3, p. 438.
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BACTERIOLOGY OF THE BLOOD.¹

BY

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EXPERIMENTAL studies in many infections, as well as collated bedside and clinical laboratory investigations, have paved the way to give bacteriology, and especially bacteriological inquiry as to the condition of the blood in disease, their proper values as diagnostic aids that the clinician no longer can afford to ignore. This paper is intended to give, briefly, recorded findings that may aid in such diagnosis, to bring together isolated reports bearing upon the mycoses of the blood, and includes a report of illustrative cases. The reported studies, both clinical and experimental, are so indexed that often they are overlooked in a most careful study of the literature, and hence the writer feels free to admit that a number of reports may have escaped his effort, but believes that the most important facts are embraced in the following summary of the literature. That bacteria can gain access to the foetus through the placenta seems fully established; it is not, however, the purpose of the writer to consider in detail the transplacental infections, but to review only those that seem to establish hæmal infection in the mother as proved by transmission of disease to the foetus.

Bacteræmia, or bacteria in the blood, is an essential phenomenon in some diseases, as, so far as is known, they do not occur except by microbic invasion of the circulating medium; relapsing fever may be taken as an example of this group. In other diseases it may be an incident of the infection and by no means requisite to the production of the clinical picture or anatomical lesion; with this class belong typhoid

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and diphtheria among the medical diseases, and abscess and other restricted or localized infections properly belonging to the domain of the surgeon. Among this group blood invasion may be of frequent occurrence, as in typhoid, or rare, as in gonorrhœa; it may or may not rise to the dignity of a complication. In still other morbid processes of an infectious nature the opposite extreme is attained, and at no time is the blood known to be invaded.

The type of bacterial invasion of the blood differs in different cases. It may be a simple infection, such as streptococcæmia, staphylococcæmia, or bacillæmia. There are valid reasons for the belief that initially most blood infections are primarily simple or single, and that when actual invasion has weakened the protective powers, broken down the barriers, it is followed by secondary and tertiary infections. The frequency with which some organisms manifest a tendency to invade the blood has led to the recognition of definite, often complex, processes whose intimate association has been indicated by a single name. The infections due to the pneumococcus may be manifested by purely local phenomena, but in not a few instances multiplicity of lesions establish hæmal distribution, and the condition may quite properly be termed a pneumococcæmia, as this conception best explains the coincidence of otitis, arthritis, meningitis, etc., with or without pneumonia. Boldt¹ suggests the term acute bacteræmia for septicæmia, and chronic bacteræmia for pyæmia.

TECHNIQUE. Even a cursory review of the literature forces upon one the conclusion that until uniform technique is employed and every step of the process carefully guarded, the results must vary, or, what is much worse, mislead, and thereby throw into discredit a most important adjuvant to accurate diagnosis. The recorded failures in the earlier studies of typhoid, diphtheria, pneumonia, etc., are clearly attributable to deficient knowledge of the essentials that must be borne in mind in each particular experiment. In many instances the failure was due to the use of an inadequate quantity of blood; the infection may be grave and still the peripheral blood poor in viable bacteria. The failure may depend upon too great dilution, or the reverse. For the detection of typhoid bacilli dilution is essential, while the gonococcus may be obtained by blood-smearing the surface of a suitable medium. It is important in every instance so to adjust the technique as to cover the requirements of that particular case. Whatever method is selected surgical asepsis must accompany every step of the operation. Smears are of little value even when prepared by approved methods. Rarely is it possible by a cover-glass or slide smear accurately to classify the

¹ New York Medical Journal, January 26, 1901.

bacteria found, much less to determine the organism observed. The amount of blood included in a smear is too small and the bacteria commonly so few, that careful systematic examination may overlook them; were these objections not insurmountable, the fact that the most important evidence sought is whether living bacteria are present, and to determine this fact the culture alone can be accepted. Even when seeking organisms known not to be cultivatable, the negative evidence yielded by showing that no growths develop renders more trustworthy the findings obtained from spreads. Among the many methods recommended by systematic and current writers the following may be mentioned:

Cabot, after cleansing the flexor bend of the elbow with disinfectants, has an assistant grasp the upper arm in order to prevent the venous return and distend the large veins at the elbow. Into the most prominent of these a sterilized needle, connected with the bulb of a sterilized syringe, is plunged. When the needle penetrates the wall of the vein the blood usually flows into the bulb of the syringe. He then withdraws 1 to 2 c.c. of blood and expels it, before coagulation takes place, into a slant tube of solid blood serum in such a way that it spreads over the whole surface; a small quantity of blood or serum should collect at the bottom of the slant; the tube is then incubated. Macé prefers an iridium needle for obtaining blood for bacteriological study.

A. Castellani¹ advises the use of a few cubic centimetres of blood obtained antiseptically and mixed with large quantities of faintly alkaline broth. Three hundred cubic centimetres of broth should be used in each of five or six flasks; the large quantity of culture fluid is necessary to prevent the action of the agglutinins and bactericidal bodies that, in the undiluted blood, may lead to untrustworthy results. He advises that the flasks be incubated at 37.5° C. Kuhnau was one of the first to guard against the bactericidal property of the blood in examining for bacteria. In typhoid fever he diluted the blood with 50 c.c. of bouillon from which plates were made.

F. K. White's technique for obtaining and plating the blood differs very slightly from that of other observers. He uses an antitoxin syringe with asbestos packing, and a two-inch needle of rather small calibre; 5 c.c. of blood are withdrawn. He inoculates 0.5 c.c. into tubes of melted agar kept at 42° C. Some of these tubes are slanted, others used for plating. Besides the agar he also uses bouillon. In obtaining the blood after death, a needle three and a half inches long (after cleansing the skin) is thrust through the fourth costal interspace

¹ Centralbl. f. Bakt., etc., 1te Abt. xxxi. (1902), pp. 477-479.

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close to the sternum into the right or left ventricle of the heart, 5 c.c. of blood withdrawn and planted in culture media as just described.

Courmont and Lesieur, in cases of enteric fever, use 2 to 4 c.c. of blood in 250 to 300 c.c. of bouillon. Growth may be tardy, however, requiring sometimes five days.

Cole prefers to have the skin over the anterior surface of the arm at the bend of the elbow carefully cleansed with green soap and water, followed by alcohol, ether, bichloride (1:1000), and a hot compress soaked in the latter solution for one-half to one hour before obtaining the blood. Experience shows that the hot compress is of great importance in causing dilatation of the superficial veins. Before abstracting the blood the bichloride is removed by spraying with sterile water. He uses 8 to 10 c.c. of blood and divides this among flasks each containing 150 c.c. of bouillon, so that the dilution is from 1:75 to 1:150. The flasks are shaken thoroughly and placed in the incubator at 37.5° C. If, at the end of twenty-four hours, the bouillon is cloudy it is plated upon agar.

H. Schottmüller examines the blood for typhoid bacilli as follows: After carefully cleansing with ether a rubber bandage is rolled around the arm and about 20 c.c. of blood removed from the vein at the elbow, using a sterile Luer syringe. The blood is next passed into several tubes of liquefied agar kept at 45° C., so that to every 6 c.c. of the medium 2 to 3 c.c. of blood are added. This, after thoroughly mixing, is plated and kept at 37° C. His diagnosis in typhoid is simplified as follows: If on examination of the plates the colonies contain motile bacilli the diagnosis is positive without further examination. As a rule, no other germs of this character were found, although occasionally pseudodiphtheria bacilli were encountered, as well as staphylococci. These, he believes, are contaminations from the skin.

Auerbach and Unger use 300 c.c. of bouillon and 20 to 30 drops of blood. The blood is withdrawn from the median vein with a sterile syringe under strict aseptic precautions. After appearance of a growth in this medium, inoculations should be made upon agar, into milk and sugar bouillon. In enteric fever they further tested an eight-hour bouillon culture with a strong agglutinating serum. By this method they could establish the presence of typhoid bacilli within thirty-six hours. Unger suggests using a large quantity of blood and diluting with a greater volume of nutrient fluid media, thereby favoring the development of organisms.

H. Skipton Tracy cites the following technique pursued in a number of cases. He recommends washing the arm with soft soap, turpentine, carbolic acid (1:30), and sterilized water, in the order named. Then a bandage is tightly applied on the upper arm to distend the

veins. An exploring syringe, with a capacity of 3 c.c., is inserted into a vein immediately under the skin. The blood is expressed into a tube of sloped agar and into a tube of bouillon and incubated. Spreads made and stained by the usual methods "will disclose the organism."

Symes¹ says that not more than 0.5 c.c. of blood should be added to 10 or 15 c.c. of broth. The preference at the present day is for a liquid culture medium, preferably bouillon.

James and Tuttle² have devised an apparatus consisting of a piece of glass tubing 12 cm. in length and 6 mm. in diameter, having a capacity of 2 c.c.; one end is tapered and ground to fit a hypodermic needle (No. 42), the other end is plugged with cotton. A larger tube incloses the one described above; both ends are plugged with cotton, and the whole apparatus sterilized by dry heat. When ready for use the inner tube is removed, the needle introduced into the vein, which is made prominent by pressure, and the blood collected.

After repeated observations clearly establishing the unreliability of superficial preparation, Prof. Coplin has formulated for use in the laboratories of the Jefferson Medical College Hospital the following elaboration and extension of Sittmann's method:

The bend of the elbow and the upper half of the forearm and lower half of the arm are washed with hot water and soap, using a stiff sterile brush; this is followed by sterile water and alcohol (60 per cent.) to remove the soap, and the preliminary disinfection is concluded by applying over the area a sterile gauze wrung out of a hot 1:1000 aqueous solution of corrosive sublimate; after twenty-four hours this dressing is removed, the arm again cleansed with alcohol and ether, followed by hot 1:1000 bichloride, and lastly with sterile hot water or normal salt solution. The use of hot solutions is important, as they not only dilate the vessels, as pointed out by Cole, but stimulate the sweat and sebaceous glands, inducing increased secretion, and thereby flushing out the ducts. The median vein of the arm is made prominent, cut down upon, fully exposed, and the skin drawn to either side out of the field of operation; a sterile hypodermic needle of large calibre or a trocar and canula, or an aspirating needle is introduced and the required quantity of blood allowed to flow into the culture vessels used and into a sterile tube. As much as 20 c.c. of blood should be obtained, certainly less than 5 c.c. must be considered insufficient in any case. Plates should be prepared according to the method advised by Schottmüller and given above. Bouillon in flasks should be inoculated, following the directions given by Cole. Agar, and also serum slants, should be inoculated as recommended by Cabot. Make spreads on cover-glasses or slides and inoculate at once at least 5 c.c., prefer-

¹ British Medical Journal, September 14, 1901.

² Med. and Surg. Reports of the Presbyterian Hospital, New York, 1898, vol. iii.

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ably more, into a rabbit, or guinea-pig, or both. A sterile test tube containing some of the blood withdrawn should be incubated with the other inoculated media. It will be observed that each step is a control to others; the plates may render it possible to determine the number of viable bacteria per cubic centimetre. The bouillon permits dilution under favorable conditions; the solid media may be adapted to special circumstances—*e. g.*, urine agar or human blood-serum agar for the gonococcus, blood-smear agar for the bacillus influenzæ, etc. The exigencies of general or hospital practice may demand haste and preclude the confessedly somewhat elaborate preparation and execution advised, but any marked deviation from the method outlined must militate against obtaining trustworthy results.

Spreads made at the time the blood is taken from the vein can be fixed and stained with any of the ordinary aniline dyes, as methylene blue, gentian violet; in fact, any of the usual laboratory dyes, or by special methods selected for the purpose of differentiating bacteria supposed to be present. Gunther's¹ method consists in immersing the spreads in a 5 per cent. aqueous solution of acetic acid for ten seconds until the hæmoglobin has faded, after which the acid is removed by briskly blowing upon the cover. The spread is then held, film downward, over the open mouth of a bottle containing ammonia, which neutralizes any residual acid. The film is then stained with the Ehrlich-Weigert aniline-oil-gentian-violet solution for twenty-four hours, after which it is decolorized with a 1 : 14 solution of nitric acid until the color fades to a light green; then rinse in alcohol, dry in air, and mount in balsam. This method removes the erythrocytes and gives a very clear field for the study of bacteria.

Review of the Literature, with Special Reference to the Modern Application of Systematic Bacteriological Examination as an Aid to Clinical Diagnosis.

Da Costa² mentions the following organisms as having been isolated from the circulating blood by different observers: *B. anthracis*, *B. coli communis*, *B. influenzæ*, *B. lepræ*, *B. mallei*, *B. pestis*, *B. tetani*, *B. tuberculosis*, *B. typhosus*, meningococcus, pneumococcus, staphylococci, streptococci, and gonococcus. In rheumatic fever Triboulet found diplococci, and Achalme, bacilli. Afanassiew observed peculiar bacilli in relapsing fever; Craig, diplobacilli in mumps; Class, Baginsky, and others have found diplococci in scarlet fever, and Balfour and Potter, diplococci in typhus fever. The spirillum of relapsing fever was demonstrated in the blood by Obermeier.

¹ *Forsch. d. Med.*, 1885, vol. iii. p. 775. Quoted by Da Costa.

² Da Costa. *Clinical Hæmatology*, 1901, p. 111.

To the foregoing Macé adds the *B. pyocyaneus*, *B. enteritidis*, *B. proteus vulgaris*, *B. botulinis*, *B. pneumonia* (Friedländer), *B. oedematis maligni*, and the *micrococcus tetragonus*.

As the *B. anthracis* was observed by Pollender (1849) in freshly drawn blood, it may be mentioned first. Blumer and Young¹ isolated the bacillus anthracis in cultures and found the organism in spreads made from a case of anthrax. D. Morisani² records an instance of anthrax in a pregnant woman; the foetus was stillborn, but no cultures were obtained from its tissues. S. Romano³ reports the case of a pregnant woman who, while suffering from malignant pustule, gave birth to a healthy child. F. Marchand⁴ records a case where, the mother suffering from anthrax, the infant developed the malady. Bacilli were found in the intervillous spaces of the placenta. Infection of the infant may have occurred in the act of birth, but the avenue of maternal infection could not be determined.

M. J. Rostowzew⁵ reports three cases of malignant pustule affecting pregnant women at the eighth, seventh, and fourth months, and proving fatal a few days after the expulsion of the uterine contents. The bacillus of anthrax was found in the placental intervillous spaces and in the fetal villi. In one case there were hemorrhages into the placental substance; in another, areas of coagulation necrosis were observed, from which the bacillus was isolated. Rostowzew found the organisms in the liquor amnii. Some organisms were recognized in the blood, but they stained poorly, being possibly in a more or less inactive stage.

The following observation by two French authorities is a very interesting one as regards tuberculosis, and if the conclusions are to be relied upon, it seems reasonable to suppose that the tubercle bacillus should be present in the circulating blood at some period of the malady. Fournier and Beaume⁶ conclude that the tubercle bacillus was present in the urine in all cases of acute tuberculosis that they examined. They urge that finding the organism in the urine possesses diagnostic value. The kidney need not be tuberculous.

The disease must be rapidly progressing, but the lesion may be in the lung or serous membranes (pleura or meninges). Anchi and Chamberlent⁷ report a case of tuberculosis in a fetus delivered between the sixth and seventh months. The mother died three days after confinement, and tubercles were found in the lungs and all the abdominal viscera. Tubercles were also present in the viscera of the foetus,

¹ Johns Hopkins Hospital Bulletin, 1895, vol. vi. p. 127.

² Morgagni, 1886, vol. xxviii. p. 523.

³ Ibid., 1888, vol. xxx. p. 458.

⁴ Arch. f. Path. Anat., 1887, vol. cix. p. 86.

⁵ Zeit. f. Geburtsh. u. Gynäk., 1897, vol. xxxvii. p. 542.

⁶ La Méd. Mod., December 4, 1902, p. 397.*

⁷ Arch. de Méd. Exper. et d'Anat. Path., 1899, vol. xi. p. 521.

together with "an enormous quantity of Koch's bacilli." Rabbits inoculated with fragments of the liver and lung of the infant exhibited tubercular manifestations two months later. Two cubic centimetres of blood from the umbilical cord were injected into the peritoneal cavity of another rabbit; this animal died in a year; tubercles were demonstrated in the peritoneum, mesenteric glands, liver, spleen, and lungs, with bacilli in all the lesions.

Jakowski,¹ in 7 of 9 cases of pulmonary phthisis, found streptococci and staphylococci; Hewelke, in 14 out of 27 cases, found staphylococci in 7, while in the remaining 7 unknown or non-pathogenic organisms were observed. Schabad, in 6 of 7 cases, found staphylococci; Petruschky, obtaining blood by wet-cups in 8 cases, found streptococci and staphylococci in only one; Straus obtained purely negative results in 19 cases. Sittmann, in 5 cases, using 2 c.c. of blood for cultures, found staphylococci in one, while the others were practically negative. Kraus obtained staphylococci in but one case out of 14. Hirschloff in 35 cases found bacteria (variety not mentioned) in only 4. Lasker,² in a series of 68 cases of the same disease (blood from the vein of the arm), found in one streptococci, in another white staphylococci. In several other cases in which colonies developed the observer attributes them to impurities. He used glycerin-agar as a medium. Barbier and Pollener³ report a case in a child, aged three years, where no macroscopic or microscopic lesions were observed, yet portions of the lung inoculated into guinea-pigs produced tuberculosis. They conclude that the results obtained could only be accounted for upon the supposition of an intense toxæmia, possibly a bacillæmia, the latter being unattended with the formation of tubercles in any of the tissues. Charrin,⁴ before the discovery of the tubercle bacillus, reported a case of foetal tuberculosis in which the lesions in the mother were principally thoracic, while in the infant (born prematurely at the seventh month) the lesions were principally abdominal.

Our views concerning blood infection in typhoid have been radically changed within the last few years. Practically all text-books on bacteriology accept the older view that the typhoid bacillus rarely invades the circulating blood—a view that has been shown to be incorrect by recent observations and indicated by earlier workers to be fallacious.

P. Ernst⁵ was the first to observe the typhoid bacillus in the blood of the living fœtus. The infant lived ninety-three hours, and the organism was found, post-mortem, in the spleen, brain, and marrow of

¹ Journal of Tuberculosis, April, 1901, p. 165.

² Deutsche Aerzte-Zeitung, January 15, 1901.

³ La Tuberculose Infantile, August 15, 1900.

⁴ Mém. et Compt. rend. Soc. de Méd. de Lyon, 1873, vol. xiii. pt. 2, p. 65, 1874.

⁵ Beiträge zur path. Anat. u. zur allg. Path., 1890, vol. viii. p. 188.

the femur. W. Fordyce¹ found in a five months' foetus, soon after delivery, from a woman dying of typhoid fever, the typhoid bacillus in the kidney, spleen, and intestinal contents, but not in the blood. V. Frascani² made careful examinations of three foetuses from women suffering with typhoid. In only one he found the typhoid bacillus in the placenta, but not in the foetal organs. C. J. Eberth³ was able to demonstrate the presence of the typhoid bacillus in the blood, spleen, and placenta of a stillborn foetus. T. Janiszewski⁴ reports a case of congenital typhoid fever, the patient living fifteen days. In this case, as well as that observed by Freund and Levy,⁵ there were no special localizations of pathological processes, but a general blood infection by the typhoid bacillus. Resinelli⁶ obtained negative results from cultures made from a foetus, the mother having typhoid. Hildebrandt⁷ also observed the typhoid bacillus in an infant.

Neuhaus⁸ reports a case of enteric fever with abortion at the fourth month of pregnancy. From the lungs, spleen, and kidneys of the foetus, typhoid bacilli were obtained. Horton-Smith⁹ isolated the typhoid bacillus from the foetal heart and spleen in a foetus four months old. The identity of the organism was established both by cultures and by Widal's reaction. Frascani¹⁰ cultivated the typhoid bacillus from the lungs of an eight months' foetus born during typhoid fever five weeks after the patient's admission to the hospital. Cultures taken from the spleen of the mother by means of a hypodermic syringe developed the same organism. Balp¹¹ reports the abortion of a foetus six months advanced, during the fifth week of typhoid fever. In the spleen and liver of the foetus the typhoid bacillus and yellow pus cocci were found. Speier¹² isolated the typhoid bacillus from a foetus which was aborted on the twenty-first day of typhoid fever, in the fourth month of pregnancy.

Bolton¹³ was successful in cultivating the typhoid bacillus from the gall-bladder and spleen of a five months' foetus extruded upon the twenty-ninth day of typhoid. In a child dying nine days after delivery, Blumer¹⁴ was able to isolate the typhoid bacillus from the umbilical cord, lung, bile, and spleen, while inoculations made from the heart, liver, and kidneys remained sterile. From two foetuses,

¹ Transactions of the Edinburgh Obstetric Society, 1898, vol. xxiii. p. 90.

² Rev. gen. Ital. di clin. Med., 1892, vol. iv. pp. 282, 343.

³ Fortschr. d. Med., 1889, vol. vii. p. 161.

⁴ Münch. med. Woch., 1893, vol. xl. p. 705.

⁵ Berlin. klin. Woch., 1895, vol. xxxii. p. 509.

⁶ Ann. de Obst. e gynec., 1896, vol. xviii. p. 695.

⁷ Fortschr. d. Med., 1889, vol. vii. p. 889.

⁸ Berlin. klin. Woch., June 14, 1886, No. 23, S. 389.

⁹ Lancet, March 31, 1900, p. 911.

¹⁰ Rivista Gen. Ital. di Clin. Med., 1892, No. 4, p. 282.

¹¹ Gaz. Med. Lombarda, 1891, vol. li. p. 396.

¹² Inaug. Dissert., Breslau, 1897.

¹³ Journ. of Path. and Bact., February, 1901, vol. vii. p. 137.

¹⁴ Journ. Amer. Med. Assoc., December 29, 1900, p. 1674.

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Richardson¹ was able to cultivate the typhoid bacillus. In one he obtained it from the liver, while in the second he was able to isolate the organism from the heart, liver, and kidney. Lynch² mentions two cases of typhoid fever occurring in pregnant women who aborted (month not stated). From the foetus of the first case he was able to cultivate the typhoid bacillus from the liver, heart, and heart's blood, although examination of the mother's blood upon three occasions proved negative. In the second case the child lived seven days in an incubator. The bacillus coli communis was cultivated from the heart's blood and foetal organs. No typhoid bacilli were demonstrable in the placenta or foetal vessels.

Hewlett,³ in 125 cases of enteric fever, isolated the bacillus of Eberth from the blood in 90. Richardson⁴ isolated the typhoid bacillus from the rose spots in 13 out of 14 cases of enteric fever. He first disinfected the area, then applied ethyl chloride, made a crucial incision in the spot and inoculated with the blood thus obtained. Quite a number of spots were examined. Lesieur⁵ states that he has found the typhoid bacillus in each of 36 patients suffering with typhoid. In 6 the serum reaction was negative; he regards the search for the bacilli of more value than the serum reaction. The technique is less easy and demands from thirty-six to forty-eight hours.

Courmont⁶ constantly found in the blood of patients having a severe or moderate form of typhoid fever the bacillus typhosus. It is usually present as early as the fifth day, and persists until the end of the third week. In prolonged cases or relapses it remains longer, but this is not constant. He further states that the presence of the typhoid bacillus in the blood has no relation to the sero-reaction, because this can be positive only later, although the organism exists in the blood from the fifth day. Courmont and Lesieur⁷ confirm the conclusions of their earlier work in typhoid fever. Of 37 cases (medium or grave) in adults, they have shown that the bacilli are present in the blood from the first days to the end of the third week. In the discussion which followed the presentation of the papers just mentioned, Widal stated that in five light cases examined between the fifth and twelfth days of the disease, the bacilli could not be demonstrated in the blood. In 20 cases (medium or grave) the bacilli were found in 17 some time between the fifth and fifteenth days. In 11 out of 15 cases of enteric fever, Cole⁸

¹ Journ. Boston Soc. Med. Sci., December 4, 1900, vol. v., No. 4, p. 116.

² Johns Hopkins Hospital Reports, 1902, vol. x., Nos. 3, 4, 5.

³ Medical Record, November 30, 1901.

⁴ Philadelphia Medical Journal, March 3, 1900.

⁵ Soc. Med. des Hôpitaux de Lyon, Seance, November 7, 1902; also Gaz. Hebd. de Med. et Chir., November 27, 1902, p. 1128.

⁶ Semaine Med., 1902, No. 1.

⁷ Soc. Med. des Hôpitaux, December 5, 1902; also La Med. Mod., December 10, 1902, p. 407.

⁸ Johns Hopkins Hospital Bulletin, 1901, vol. xii. p. 203.

was able to identify the typhoid bacillus not only by the appearance of plate colonies, but by subcultures on different media, and finally agglutination by known typhoid serum in dilution of 1 : 50 in one hour. The positive results were obtained at various stages of the disease, mostly during the second week ; earliest on the sixth day and latest on the twenty-seventh day, the latter being on the second day of an intercurrent relapse. In five cases the cultures were positive before a satisfactory Widal reaction was obtained. F. G. Harris and E. K. Kerr¹ report finding the typhoid bacillus in the blood in 31 of 56 cases. All observers agree that the cultures are positive before the Widal reaction is obtained.

Warfield² reports a case of typhoid fever in a child, aged twelve years, having had three relapses. From the blood a pure culture of the typhoid bacillus was obtained. In two cases of enteric fever, Stacey³ obtained the typhoid bacillus from the blood in both. In three series of cases Schottmüller⁴ was able to diagnose enteric fever by examination of the blood before the clinical diagnosis had been made. As early as the second to the fifth day motile bacilli were observed in plates made by the procedure recommended by him. In the first series of 50 cases observed in 1899, he isolated the bacillus in 40 cases (80 per cent.) ; in the second series of 61 cases in 1900, the organism was found in 58 cases (84 per cent.) ; and in 1901 and 1902 in 101 cases he obtained positive results in 84 per cent. He considers it proper to regard each case of typhoid as a specific bacteremia, and that it is probable the bacilli reach the blood through the inflamed mesenteric glands. As regards the number of colonies per 100 c.c. of blood examined he has found from 5 to 2020. In cases where remittance or recrudescence of the fever had taken place no bacteria were found in the circulation. Auerbach and Unger,⁵ in 10 cases of typhoid fever, observed the bacillus typhosus in 7. In their seven positive cases they found the bacillus typhosus in

3 cases upon the	12th day.
1 case " "	16th "
1 " " "	22d "
1 " " "	29th "
1 " " "	42d "

Schottmüller,⁶ from a case which in some respects clinically resembled typhoid fever, withdrew 20 c.c. of blood, mixed it in six tubes of liquefied agar and plated. In forty-eight hours thirty-four colonies were visible, mostly situated in the depth of the medium ; they were

¹ Paper read before the Chicago Pathological Society, October 1, 1902.

² Johns Hopkins Hospital Bulletin, July, 1902.

³ Australasian Med. Gazette, October 20, 1902, vol. xxi., No. 10.

⁴ Münch. med. Woch., September 23, 1902.

⁵ Deut. med. Woch., December 6, 1900.

⁶ Ibid., August 9, 1900.

of a blackish-green color, while the few upon the surface were of a mouse-gray color. He states that these peculiar colors of the superficial and deep colonies are characteristic of typhoid and typhoid resembling bacteria in blood cultures, and apparently due to the change of the blood-coloring matter by the growing bacteria. The colonies contained rods which in hanging-drops showed the form and motility of the typhoid bacillus. They decolorized by Gram's method. Culturally the organism resembled the typhoid bacillus, with the exception that it fermented sugar bouillon. It was also negative to Widal's test in dilutions of 1 : 100, 1 : 50, and 1 : 20 with serum from a typhoid patient, but agglutinated perfectly with the patient's serum in dilution of 1 : 50 and 1 : 20. After subsidence of the fever the serum reaction was again tried in dilution of 1 : 100 ; it gave a clearly defined agglutination with the bacillus. He concludes from the examination of this case that the infection was due to a bacillus closely resembling the typhoid and the colon group of organisms, and that there are cases which clinically are like typhus abdominalis, but not due to the typhoid bacillus. Gwyn¹ isolated from the blood a paracolon bacillus in a case which closely resembled the one observed by Schottmüller. Johnston,² Longcope,³ Coleman and Buxton,⁴ and Cushing⁵ have also isolated typhoid-like bacilli from the blood in cases clinically resembling typhoid fever. The most conspicuous difference in the organism isolated in all these cases is its non-agglutination with typhoid serum. Hewlett,⁶ in a case similar to that of Gwyn, isolated from the blood a bacillus which agglutinated with the patient's serum in dilutions of 1 : 100, and did not agglutinate with typhoid serum.

Canon⁷ states that it is now a routine practice at the Moabit Hospital at Berlin to draw 2 to 5 c.c. of blood from the median vein and sow it on agar or bouillon, or to inoculate animals in every case of blood poisoning, progressive phlegmon, or general sepsis. This examination is made as early as possible and the number of colonies that develop is recorded. He has been impressed with the fact that the finding of staphylococci is less important than when streptococci are encountered, especially when the staphylococcus infection is an osteomyelitis.

Kohn,⁸ in a case of sepsis following osteomyelitis, and using 10 c.c. of blood inoculated into serum-glucose-agar and glucose bouillon obtained entirely negative results. In a second examination 15 c.c.

¹ Johns Hopkins Hospital Bulletin, 1898, vol. ix. p. 54.

² THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, August, 1902.

Ibid., August, 1902.

⁴ Ibid., June, 1902.

³ Johns Hopkins Hospital Bulletin, 1900, vol. xi. p. 156.

⁶ THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, August, 1902, p. 206.

⁷ Mitteilungen a. d. Grenzgebieten (Jena), vol. x. pp. 3-4.

⁸ Medical Record, January 17, 1903.

of blood were used, and in glucose bouillon the staphylococcus pyogenes aureus was obtained.

Von Eiselberg¹ shows that the blood in cases of sepsis does not contain as many bacteria during life as immediately after death, when cultures are made directly from the heart. Of 156 cases of sepsis examined, in 77 the specific organism was found in the blood during life; in 70 cases only after death could the organisms be found in the heart's blood, while in the remaining nine cases no bacteria were found during life or at post-mortem. The organisms encountered were the streptococcus, staphylococcus, pneumococcus, gonococcus, and bacillus coli communis. In three cases of puerperal septicaemia, Stacey isolated the streptococcus pyogenes in one, and the staphylococcus albus (? streptococci) in the other two. In cases of sepsis Bonnaire² mentions three instances in which streptococci seem to have passed from the mother to the foetus by the placental route. In sepsis neonatorum the streptococcus, staphylococcus, bacillus coli communis, bacillus enteriditis of Gärtner, and a bacillus analogous to the bacillus of Friedländer, have been isolated by different investigators. Barrows,³ in a case of puerperal septicaemia, isolated the streptococcus pyogenes from the circulating blood. F. K. White,⁴ in 18 cases of sepsis, chiefly of local septic infection without the formation of metastatic abscesses, found in 37 blood cultures made during life specific bacteria only four times. The streptococcus pyogenes was found in pure culture three times, and the staphylococcus pyogenes aureus in pure culture once. Fifty to sixty colonies of streptococci were obtained from 1 c.c. of blood.

C. Bidone⁵ mentions an instance of a pregnant woman attacked by facial erysipelas, who gave birth to a child at full term. She died in the puerperium from septic peritonitis and endometritis. The infant died nineteen hours after birth, and at autopsy vegetations were found on both tricuspid and mitral valves, but especially on the former. Numerous streptococci were found in the spleen, lungs, and kidneys, but more particularly in the vegetations on the cardiac valves. Cultures and inoculations showed that the micro-organism was the streptococcus of erysipelas.

Achalme⁶ found that streptococci were present in great numbers in the connective tissue separating the lobules of fat in the subcutaneous structures and in the walls of the lymphatics in cases of erysipelas neonatorum. G. Ricker⁷ reports two cases in which the streptococcus pyogenes was found in the foetus. In one case the mother died from diphtheria, and the streptococcus was found in her body, in the pla-

¹ Wiener klin. Woch., 1890.

² L'Obstetrique, 1899, vol. iv. p. 473.

³ New York Medical Journal, January 31, 1903.

⁴ Journ. Exp. Med., May and July, 1899, Nos. 3-4, vol. ix. p. 425.

⁵ Teratologia, 1894, vol. i. p. 182.

⁶ Thèse de Paris, 1892.

⁷ Centralbl. f. allg. Path. u. path. Anat., 1895, vol. vi. p. 49.

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centa, and in the liver of the foetus. In the second, the mother suffered from an abscess of the arm, which proved fatal after the delivery of a stillborn infant, which showed the streptococcus in the blood of the umbilical vein.

Da Costa claims that in erysipelas bacteriological examination of the blood is usually negative. Pfahler¹ has isolated a diplococcus quite constantly from the blood of the area involved in cases of this disease. Ballantine says that streptococci apparently sometimes pass the placental barrier and invade the foetal tissues by the umbilical avenue of entrance. They must, then, reach first the organs, such as the liver and heart; and there is evidence to show that they may set up morbid changes in these parts without affecting the skin or subcutaneous tissue at all. This latter is true of variola, in that not having the pustules of the disease externally there may have been secondary infection by staphylococci and streptococci.²

In croupous pneumonia the pneumococcus is frequently found in the circulating blood. In numerous cases of pneumococcic arthritis various observers seem to have established fully that the organism reaches the joints by way of the blood. Prochaska³ concludes from his study that in all cases of pneumonia a careful examination would demonstrate the presence of bacteræmia, and mentions in another report⁴ that he isolated the diplococcus of pneumonia from the blood in four cases of pneumococcus sepsis. Cole⁵ believes that in severe cases the pneumococci are either more numerous or more resistant, and does not agree with Prochaska, that the number of pneumococci in the blood has no relation to the severity of the attack. G. Carbonelli⁶ records a case of pneumonia in a foetus which showed diplococci in the blood, spleen, and peritoneal exudation, while the mother had suffered from no infectious disease during her pregnancy. Netter records a case of pneumonia where pneumococci passed from the mother to the foetus. Stacey, in 17 cases of croupous pneumonia found the pneumococcus in the blood in 7 cases, and in only 3 of these before death. Silvestrini and Sertoli⁷ found the diplococcus of pneumonia in the blood in 15 of 16 cases examined. Beco reports one case of pneumonia due to Friedländer's bacillus in which there was a general bacillæmia. Baudel claims that in pneumonia the number of organisms (diplococci) bears a relation to the gravity of the local process. He further claims that the diplococcus may localize itself in the blood primarily or secondarily, and that the persistence of the organism in the blood is a common phenomenon and

¹ Philadelphia Medical Journal, April 19, 1902.

² Anche. Bull. Soc. d'Anat. et Physiol. de Bordeaux, 1892, vol. xlii. p. 278.

³ Deut. Arch. f. klin. Med., Band lxx., Heft 5 and 6.

⁴ Deut. med. Woch., May 22, 1902.

⁵ Johns Hopkins Hospital Bulletin, June, 1902.

⁶ Riv. di Ostet. e gynec., 1891, vol. li. p. 281.

⁷ Nothnagel's Practice, Diseases of Bronchi, Lungs, and Pleura, pp. 417, 418.

not a complication to be dreaded. E. Phillipi¹ reports a fatal case of lobar pneumonia in which Friedländer's bacillus was cultivated from the blood during life and was obtained from the pulmonary lesions at autopsy. The pneumococcus was not obtained from the pulmonary lesions.

F. K. White, in 19 cases of lobar pneumonia, all at least moderately severe, obtained the diplococcus of pneumonia only three times during life in fatal cases. In 8 negative cases which were autopsied pneumococci were found in the lung, but there was no evidence of a general infection. No organism save the pneumococcus was found in the blood in any case. Only ten to sixty colonies were observed per cubic centimetre.

In influenza Canon² found a number of short bacilli in the blood of twenty cases; while Pfeiffer and Ruhnau³ obtained negative results. Jehle⁴ obtained cultures of the bacillus of influenza in cases of diphtheria, pertussis, scarlet fever, measles, and varicella. He believes that these diseases predispose to an influenzal bacteræmia.

Hunter and Nuttall,⁵ in discussing the bacteriology of cerebro-spinal meningitis, state that Gaucher, in 1881, demonstrated the presence of micrococci in the blood. Salomon⁶ does not accept the positive view of Marx, that meningitis due to the meningococcus is always a blood infection by way of the tonsils, but reports an instance in which the coccus was obtained from the blood and cerebro-spinal fluid during life. Jager has found the organism in the spleen, kidneys, and pericardium. In Salomon's case the coccus was present in the blood some time before it was localized in the meninges, hence the meningitis was predicted and confidently awaited. Stacey obtained negative results in one case of epidemic cerebro-spinal meningitis.

Gwyn⁷ reported a case of epidemic cerebro-spinal meningitis from which he isolated the diplococcus intracellularis during life from the blood as well as from fluid obtained by spinal puncture and from fluid aspirated from an inflamed joint. In 8 cases of cerebro-spinal meningitis, 6 of which were fatal, F. K. White found no pathogenic bacteria in blood cultures. In 5 cases blood cultures were made shortly after death, and all proved sterile. Gradwohl⁸ details a very interesting account of a mother affected with epidemic cerebro-spinal meningitis transmitting the disease to a seven months' fœtus which, owing to the death of the mother, remained undelivered. Bacteriological examination of fluid from both the maternal and fœtal meninges revealed the

¹ Münch. med. Woch., November 11, 1902; Medical Record, Dec. 6, 1902, p. 909.

² Coles. The Blood, 1902, 2d ed. p. 246.

³ Deut. med. Woch., 1893, vol. xix. p. 816.

⁴ Zeit. f. Heilk., 1901, vol. xxii. p. 190.

⁵ Lancet, June 1, 1901.

⁶ Berlin. klin. Woch., November 10, 1902.

⁷ Johns Hopkins Hospital Bull., 1899, vol. x. p. 112.

⁸ Philadelphia Monthly Medical Journal, July and September, 1899, vol. i.

meningococcus, which was also isolated in pure culture from the left ear of the mother. In a sporadic case of epidemic cerebro-spinal meningitis in a pregnant woman, Herwerden¹ isolated the pneumococcus from the meninges of both mother and foetus.

Mary Hamilton-Williams² relates cases occurring among East African coolies in which the diplococcus intracellularis was found eighty times in both sweat and blood. In two cases of epidemic cerebro-spinal meningitis in pregnancy studied by P. Foa and G. Bordoni-Uffreduzzi,³ the mothers suffered from pneumonia, stage of red hepatization. The foetuses expelled at the fourth and sixth months, respectively, showed in their blood and in the liver the diplococcus of pneumonia.

Letzerich⁴ isolated from the blood in three cases of purpura hemorrhagica a bacillus resembling the anthrax bacillus. Inoculation into animals was followed by the same hemorrhagic condition noticed in the human being. This observer himself suffered with the malady, and from his own blood was able to cultivate the same bacillus and produce the same lesions in the lower animals.

Ehrlich⁵ mentions that in a case of purpura he was able to obtain the staphylococcus pyogenes aureus from the blood. Hryntschalk⁶ was unable to find bacteria in the blood of these cases. Schram and Rubovits,⁷ though unable to demonstrate bacteria in the blood in a case of purpura hemorrhagica during life, nevertheless observed numerous micrococci in the walls of the bloodvessels in the tissues examined. In purpura transmitted from mother to foetus, Diehl⁸ could not demonstrate the presence of micro-organisms in the organs of the mother or child, though a very careful examination was made. V. Hanot and Ch. Luzet⁹ report a similar case, although they found the streptococcus pyogenes in the petechiæ on the pericardium and liver.

Stacey, in 3 cases of acute infective periostitis and osteomyelitis, found the staphylococcus aureus in pure culture in the blood and in the pus of all the abscesses. In 6 cases of cellulitis organisms were found in the blood in every case. In 3, staphylococcus aureus, in 1 streptococcus, in 1 staphylococcus albus (? streptococcus), and in 1 the staphylococcus aureus during life, but after death the staphylococcus albus and a streptococcus.

Cole¹⁰ mentions a case of infection by the bacillus aërogenes capsulatus

¹ Schmidt's Jahrbuch., 1893, vol. iv. p. 227.

² Journal of Trop. Med. Quoted by J. Rutter Williamson, A Clinical Study of Epidemic Cerebro-spinal Meningitis, Calcutta, 1901. The original reference could not be verified.

³ Deut. med. Woch., 1886, vol. xii. p. 249.

⁴ Untersuchungen über die Kenntniss der purpura hemorrhagica. Leipzig, 1883.

⁵ Charité Annalen, 1884.

⁶ Archiv f. Kinderheilkunde, 1884.

⁷ Philadelphia Medical Journal, August 16, 1902.

⁸ Zeitschr. f. Geburtsh. u. Gynäk., vol. xli. p. 218.

⁹ Arch. de Med. Exper. et d'Anat. Path., 1890, 18. vol. ii. p. 772.

¹⁰ Johns Hopkins Hospital Bulletin, October, 1902.

in which the organism was demonstrable in the blood during life. About 8 c.c. of blood were withdrawn, 1 c.c. of which was introduced into the ear of a rabbit. The remainder of the blood was placed in twelve tubes of litmus milk. The rabbit was killed after a few minutes had elapsed and placed in the incubator. Twenty-four hours later the rabbit was found to be distended with gas, and crepitus could be made out over the abdomen. Cover-slips made from the liver, spleen, and heart's blood showed the presence of an organism morphologically identical with the bacillus described by Welch and Nuttall. The cultures in milk were also typical of the organism, showing acidification, with coagulation and gas bubbles upon the upper surface of the clot.

Gwyn¹ also isolated the bacillus *aërogenes capsulatus* during life in a case of chorea insaniens and acute endocarditis. He was able on three occasions to demonstrate this organism in the circulating blood both by cover-slip and by culture, the first time thirteen days before death.

Blum,² in a case of malignant endocarditis, isolated the bacillus *pyocyaneus* from the blood before death and one from the heart's blood one and one-half hours post-mortem.

Harris and Johnston³ cite a case of gonorrhœal endocarditis from which the gonococcus was isolated. Twelve cubic centimetres of blood were divided among four Erlenmeyer flasks, each containing 150 c.c. of bouillon, to which 20 to 30 c.c. of hydrocele fluid had been added. On two other occasions 12 c.c. of blood were mixed with 25 c.c. of melted agar and immediately plated. In each instance the media remained sterile. Twenty-four hours before death the median basilic vein was exposed under cocaine anæsthesia and 12.5 c.c. of blood removed and divided among three tubes, each containing 10 c.c. of melted agar, which was plated, and two slanted hydrocele-agar tubes in which there was an excess of hydrocele fluid. A second 12.5 c.c. of blood was divided among three 150 c.c. flasks of bouillon and one 150 c.c. of litmus milk. Both *aërobic* and *anaërobic* methods of cultivation were employed. In the *anaërobic* cultivations only one colony made its appearance up to seventy-two hours in an agar plate.

In the *aërobic* cultivations growths were evident in plates of agar and those of hydrocele fluid agar. The flasks containing bouillon remained sterile. Spreads made at random from colonies upon all the media showed in every instance a diplococcus never definitely biscuit-shaped, often lance-shaped, and frequently irregular in size and form. They were decolorized by Gram's method. A marked viscosity was characteristic of all the colonies. Of fourteen plain agar tubes inocu-

¹ Johns Hopkins Hospital Bulletin, 1900, vol. xi, p. 185.

² American Medicine, January 17, 1903.

³ Johns Hopkins Hosp. Bull., October, 1902.

lated, a few minute colonies developed upon two. On a mixture of human blood and agar they grew luxuriantly, some of the colonies reaching 2 mm. in diameter. It could not, however, be cultivated beyond the second generation. No inoculation experiments were made. At autopsy gonococci were obtained from the heart's blood; streptococcus pyogenes from the kidney, urinary bladder, and urethra; bacillus coli communis from the heart's blood, kidney, and urinary bladder.

The above-mentioned observers give the following references to cases of gonorrhœal endocarditis and the results obtained culturally:

Thayer and Blumer¹ isolated the gonococcus from the blood upon a mixture of blood (one-third) and melted agar (two-thirds). Thayer and Lazear² obtained the organism upon melted agar; Byelogyw³ was also successful in cultivating the gonococcus from the blood upon glycerin-hydrocele-agar; and R. J. Wilson⁴ was able to isolate the gonococcus in two cases, one upon glucose agar and plain agar, and the other upon plain agar. The amount of blood used varied from 1 to 5.5 c.c.

Unger⁵ reports a case of gonorrhœal arthritis which was at first supposed to be a case of osteomyelitis. A growth of gonococci was obtained from blood withdrawn from the median vein and inoculated upon ascitic fluid.

Bacilli⁶ reports a very interesting case of acute polymyositis occurring in a man, aged thirty-nine years, in which the staphylococcus pyogenes albus was observed microscopically in the blood obtained from an incision made in removing a piece of muscle from the left leg.

In bubonic plague the bacillus is readily observed in spreads made from blood as well as obtained in cultures. Atkinson⁷ records that the bacillus pestis was found in the blood in 221 out of 273 cases. He recommends the use of a medium consisting of bouillon with 2 per cent. peptone and 1 per cent. gelatin.

Novy⁸ claims that the number of bacilli in the blood during life in cases of bubonic plague is very small, and for this reason their detection by direct microscopic examination is difficult. In the experience of the German Commission, where the cover-glass preparations gave negative results, the cultural methods were successful. Of 124 cases thus examined 81 gave negative results. Novy recommends the use of 1 or 2 c.c. of blood drawn from a vein and spread over agar tubes or over agar plates. In cultures made from the blood Stacey, "in a dozen or more" cases of bubonic plague, claims that the bacillus pestis was found in several.

¹ Johns Hopkins Hospital Bulletin, 1896, vol. vii, p. 57.

² Journ. of Exper. Med., vol. iv, p. 81.

³ Bull. Med. Sci., July, 1901.

⁴ Il Policlinico, 1902, No. 13, fasc. 1 and 2, p. 16.

⁵ THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, October, 1901, p. 417.

⁶ Bolnitch. Gaz., 1899, No. 4, p. 187.

⁷ Corres. Med. Presse, December 11, 1901.

⁸ Lancet, January 26, 1901.

W. J. Calvert,¹ in reporting 36 cases of bubonic plague, demonstrated the organism in the circulating blood obtained from the lobe of the ear in every case. In a few instances the first examination was negative, but the second was positive. In all cases smears and cultures were obtained at intervals of four hours after admission to the hospital. Smears were stained by Gram's method, then counterstained lightly with methylene blue or carbol-fuchsin, which showed to advantage the bipolar staining of the bacillus.

Within quite recent years the bacillus of diphtheria in extremely malignant cases has been isolated from the blood by several observers. Suessewein² mentions that diphtheria bacilli are frequently found in the blood in this disease. In a young man, aged nineteen years, suffering with diphtheria, Niessen³ isolated the diphtheria bacillus in pure culture from blood taken from the median vein. In one case Stacey failed to find the bacillus in the blood.

In 40 children, varying in age from a few days to four years, all believed to be suffering from infections which bade fair to end fatally, Delestre⁴ found bacteria in the blood of 14 during life. Of 8 who recovered, but one gave a positive result. The organisms found were the streptococcus, staphylococcus, pneumococcus, and colon bacillus, while influenza bacilli were isolated more rarely. He also showed that premature babies seem especially susceptible to the streptococcus and colon bacillus, while nursing infants several months old are more prone to staphylococcus infections.

Weber⁵ isolated blastomycetes during life from the blood of a child, aged two years, suffering from furunculosis. The furuncles were attended with fever; the child finally died from exhaustion. At autopsy tuberculosis of the cerebellum, lungs, and liver was observed.

Lille and Jullien⁶ claim to have isolated a bacillus from the blood of syphilitic patients. It is a short, thread-like polymorphic organism, and causes when inoculated into guinea-pigs an indurated ulcer and enlargement of the nearest lymphatic glands.

In a case of congenital elephantiasis⁷ in a child, five months old, the streptococcus of Fehleisen was isolated from the blood serum obtained from the lower third of the right leg. Examination of the mother's blood was negative.

Maragliano⁸ states that in cases of carcinoma bacteria are rarely

¹ *Centralbl. f. Bakt. Parasit. und Infektionskrankheiten*, January 26, 1903, No. 4, Bd. xxxiii.

² *Wien. klin. Woch.*, February 6, 1902.

³ *Wien. med. Woch.*, 1902, Nos. 47 and 48.

⁴ *Annal. de Gynecol. et d'Obstet.*, 1901, vol. iv. p. 51.

⁵ *Soc. of Int. Med.*, Berlin, December 1, 1902; *Gaz. Hebdom. de Med. et de Chir.*, December 18, 1902, p. 1200.

⁶ *Bull. de l'Acad. de Med. de Paris*, July 2, 1901.

⁷ *Trans. Edinburgh Obst. Soc.*, 1896, vol. xxi. p. 25.

⁸ *Gazz. degli Osped.*, January 13, 1901.

found in the blood prior to ulceration of the cancer. He believes that the mycosis of the blood is largely responsible for the cachexia of the condition, even when the bacteria are not endowed with the property of producing suppuration, but of such a low order of virulence as to interfere with nutrition only.

In *melæna neonatorum* numerous organisms have been isolated by different observers. Gärtner¹ has isolated a bacillus; others have found streptococcus alone or with the diplococcus of pneumonia; bacillus *pyocyaneus* alone or with the staphylococcus, bacillus *lactis aërogenes*, a bacillus like that of Friedländer, and a micro-organism suggesting, but not to be identified with, the diplococcus of pneumonia.

Of 37 cases of severe chronic diseases reported by White, including 11 of cardiac disease, 9 of cancer, 4 sarcoma, 3 phthisis, 3 chronic nephritis, 1 each of Pott's disease, arterio-sclerosis, tuberculous meningitis, tuberculous peritonitis, gastric ulcer, chronic rheumatism, and pernicious anæmia, only 9 gave positive results by blood culture.

In two cases of chronic nephritis (parenchymatous) thirty to fifty colonies of the streptococcus *pyogenes* per cubic centimetre were obtained during life in one, and seventy to ninety colonies of the same organism in the other. In the case of Pott's disease ten to fifteen colonies of the streptococcus *pyogenes* per cubic centimetre were found. In the case of gastric ulcer six to ten colonies of the staphylococcus *pyogenes aureus* were obtained. From a case of myocarditis and pericarditis five to eight colonies of the staphylococcus *pyogenes aureus* per cubic centimetre were isolated. Five to six colonies of the staphylococcus *pyogenes aureus* were obtained half an hour after death in a case of mitral and aortic stenosis, though during life blood cultures were negative; in a similar case, one-half hour after death, ten to twelve colonies of the staphylococcus *pyogenes aureus* were found, though three days before death cultures made from the blood were negative.

Blood cultures made two days before death in a case of cancer of the epiglottis were negative, though three-quarters of an hour after death ten to twenty colonies of the streptococcus *pyogenes* per cubic centimetre were found.

ORIGINAL CASES. The accompanying table comprises ten cases which came under the observation of the writer. He wishes, in this connection, to thank Drs. Keen, Da Costa, J. C. Wilson, and Thornton for the privilege of reporting the cases. In the technique (except Nos. 4 and 7) Coplin's modification of Sittman's method was observed, the vein of the arm made prominent and then punctured with a sterile trocar and canula. The trocar being removed, five drops of blood were thoroughly mixed with 20 c.c. of agar and several plates spread.

¹ Arch. f. Gynäk., 1893, vol. lxx. p. 272.

These were incubated, and as soon as colonies appeared they were examined at once. In Case No. 7, 1 c.c. of blood was thoroughly mixed with 50 c.c. of bouillon; the withdrawal of blood was made hurriedly, and only inadequate antiseptic precautions were observed—that is, instead of preparing the arm several hours before puncture of the vein, the arm was simply washed with bichloride solution, 1:1000, then with distilled water, and the puncture made immediately afterward. Too much stress cannot be laid upon the question of disinfecting the skin over and around the site of operation; the least laxity in this procedure will readily permit the entrance of omnipresent bacteria.

No.	Name, sex, age.	History.	Clinical diagnosis.	Result of bacteriological examination of blood.	Clinical result.
1	L. T. female, 39	Tumor in left breast, followed by two other masses in the same organ; breaking down of the first nodule, with discharge of straw-colored fluid. Excision of breast; operative recovery; sudden rise of temperature to 101.4° F. 19th day after operation.	Scirrhus of mamma; post-operative infection.	Staphylococcus pyogenes albus.	Recovery.
2	M. O'B. female, 42	History of recurrent carcinoma of breast. Irregular temperature, suggesting sepsis, beginning on day following operation, continuing twenty-seven days; blood examination on 12th day.	Recurrent scirrhus of mamma; post-operative infection.	Staphylococcus pyogenes albus and sarcina lutea.	Recovery.
3	M. Y. female, 47	For nine years has had enlargement of veins of left leg. At time of admission to hospital patient could not walk on account of pain and oedema of part. Temperature 98.2° F. Examination of blood two days before operation of ligating the veins.	Thrombophlebitis of varicose saphenous vein.	Sterile.	Recovery.
4	Mrs. N. female, 36	Three days after labor seized with headache and chills; offensive discharge from vagina. Temperature 98° to 104° F. Blood examined on the 30th day.	Puerperal sepsis with femoral thrombophlebitis.	Sterile. Single inoculation, quantity of blood insufficient.	Recovery.
5	L. H. female, 23	Pain in right iliac region. Temperature 99° F. Examination of blood two days after admission to hospital.	Salpingitis.	Sterile.	Recovery.
6	L. H. female, 23	Following an injury there appeared a growth about the size of an egg at the angle of scapula, which steadily enlarged until at time of operation measured 26 by 15 cm. Excision of mass and parts of four ribs; operative recovery, with temperature from 99° to 102.4° F. Blood examined twenty days after operation.	Sarcoma of ribs and pleura; post-operative infection.	Staphylococcus pyogenes albus.	Recovery.
7	R. H. R. male, 32	Attack of appendicitis; operation; eight weeks later complained of diarrhoea with malaise; temperature from 98° to 104.6° F. A faint systolic murmur was heard over the pulmonic area. Blood examined 4th day.	Malignant endocarditis.	Sterile.	Death.
8	M. G. female, 33	Puerperium followed by slight infection and femoral thrombophlebitis. Examination of blood made during the second week of disease.	Puerperal sepsis.	Sterile.	Recovery.
9	J. D. male, 52	Four weeks before admission to hospital had a severe chill, followed by headache, fever, sweating, and weakness. A chill every other day for a week following admission; temperature from 99° to 104.8° F. No hematозoon malarie. Examination of blood ten days after admission to hospital.	Malignant endocarditis.	Staphylococcus pyogenes albus, sarcina lutea, and an unidentified chromogenic bacillus.	Death.
10	E. I. female, 21	Following acute tonsillitis; temperature from 97.8° to 104.6° F. for two weeks. No hematозoon malarie. Three Widal tests negative. Blood examination made on 20th day of illness.	?	Sterile.	Recovery.

It will be seen from this small number of cases that bacteria were found in four (40 per cent.); of these one was malignant endocarditis and three were post-operative infections.

SUMMARY. Bacteriological examination of blood obtained from the living, under suitable conditions, may afford information, without which neither accurate diagnosis nor intelligent treatment is possible. This is particularly true of cases in which antitoxic and bacteriolytic sera are indicated.

For trustworthiness careful attention to technique is a prerequisite. When the organism thought to be present is one not readily grown upon ordinary culture media, special media should be utilized. In infection by the gonococcus, Wertheim's medium or fluid from ascites or hydrocele should be used, though Harris and Johnson and others used plain agar and succeeded in isolating the organism.

Post-mortem examination of the blood should not be relied upon to determine the nature of an infection; in many instances the results are misleading and often entirely untrustworthy. It is a well-known fact that in certain diseases organisms are not present in the blood during life, but in the period just preceding death, as shown by Longcope,¹ there is a marked progressive decrease in the bacteriolytic blood complement which permits the blood to become overwhelmed with bacteria, some of which may be harmless saprophytes. Bacteriological examination of the blood post-mortem in diseases in which bacteria are present ante-mortem, by reason of the agonal infection, usually yields only confusing results.

Transplacental infection constitutes an important element in ante-natal pathology.

In 535 collated cases of enteric fever the bacillus typhosus was demonstrated to be present in the circulating blood in over 80 per cent. Schottmüller's belief that all cases of enteric fever should be regarded as bacteræmias, seems justifiable. Observers agree that the bacillus may be demonstrated in the blood before a positive Widal reaction is obtainable. It is a well-known fact that in some typhoid patients the blood does not yield the reaction any time in the entire course of the disease. Sometimes the Widal reaction is obtained with laboratory cultures of the organism early and only later with bacilli obtained from the blood of the patient. Troussaint² records seven cases of typhoid (four fatal) in which the bacillus of Eberth was isolated from the blood when the Widal reaction was still negative. In the four fatal cases it was not obtained at all; in one non-fatal case the Widal reaction was positive on the eighth day, with laboratory

¹ Journal of Hygiene, January, 1908, No. 1, vol. III.

² La Méd. Mod., February 11, 1908, p. 44.

cultures of the bacillus of Eberth, but not positive with the bacillus obtained from the blood until the nineteenth day. Further peculiarities of reaction are illustrated by the instance in which the bacillus isolated from the blood did not agglutinate with the same blood, but was agglutinated by the blood of a rabbit immunized to the bacillus of Eberth. The results of the bacteriological examination of the blood in typhoid fever seem to place this procedure as a diagnostic aid in advance of the serum reaction. In cases of enteric fever in the fœtus, numerous instances of which are herein incorporated, the bacillus typhosus has been found in the blood and internal organs in the majority examined.

This fact also seems to prove that the disease is, often if not always, a blood infection.

In over 46 per cent. of 176 cases of sepsis various organisms were isolated from the blood obtained during life. These cases included puerperal sepsis as well as local septic processes, such as phlegmons, and cases in which the clinical diagnosis was septicæmia and pyæmia. Infective periostitis and osteomyelitis may be included with this group.

It seems probable that proper identification of the bacteria present in the blood in septic processes would reconcile discordant views as to the therapeutic efficiency of sera.

Of 58 cases of croupous pneumonia the diplococcus of pneumonia was found in the blood in 53 per cent.; the bacillus of Friedländer has been observed occasionally.

In 69 per cent. of 433 cases of bubonic plague the organism was demonstrated in blood obtained during life.

The bacillus influenzae, the meningococcus, gonococcus, and bacillus diphtheriae occur in the blood with no degree of constancy. In a number of cases of ulcerative endocarditis bacteria have been found in the blood during life. The same is true of purpura.

By methods at present available the tubercle bacillus is rarely demonstrable in the blood, although clinical and laboratory investigations indicate that it should be more readily obtained. The bacterial flora of the blood in tuberculosis are usually of secondary import, and indicate a more grave prognosis.

It has been mentioned that two observers (Lille and Jullien) isolated a bacillus from the blood serum of a syphilitic. Joseph and Piorkowski¹ also claim to have isolated bacilli from the semen and from the blood of syphilitics. Should these observations be supported by further studies, bacteriological examination of the blood may be of diagnostic value in syphilis, as already established for those complica-

¹ Deut. med. Woch., 1902, Nos. 50-52.

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tions in gonorrhœa attributable to hæmal dissemination of the gonococcus.

The writer wishes here to express his sincere thanks to Professor Coplin, Director of the Laboratories of the Jefferson Medical College Hospital, for assistance rendered in the preparation of this article.

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CHANGES IN THE INTERCOSTAL MUSCLES AND THE DIAPHRAGM IN INFECTIVE PROCESSES INVOLVING THE LUNG AND PLEURA.¹

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So far as the writer is aware, no important study has been undertaken of the relation, if any, existing between the intercostal muscles and inflammations of the lung and pleura, or of either alone. An examination of the most important text-books on medicine and pathology discloses no reference to characteristic anatomical changes in the intercostal muscles or nerves in any of the conditions under consideration.

Aufrecht,² in a most exhaustive article on pneumonia, notes the occurrence of severe intercostal pain and pain in the abdominal muscles, both of which are attributed to the cough, and this seems to be the view held by other observers. It is reasonable to assume that the cough induces muscular soreness, comparable to the soreness resulting from any other form of muscle fatigue, but, in some cases at least, muscle pain and tenderness may depend upon demonstrable lesions in the affected tissues.

Rosenbach,³ in his elaborate article on pleurisy, speaks of atrophy of the thoracic muscles and antagonistic muscles, and briefly refers⁴ to the fact that changes occur in the costal pleura and intercostal muscles during perforation.

Again,⁵ without any special detail as to the character of the lesions, he refers to degeneration of the thoracic muscles in acute

¹ Read before the Pathological Society of Philadelphia, January 28, 1904.

² *Diseases of the Bronchi, Lungs, and Pleura*, Nothnagel's Encyclopedia, 1903, p. 455.

³ *Ibid.*, p. 826.

⁴ *Ibid.*, p. 830.

⁵ *Ibid.*, p. 882.

and chronic pleurisies. The same writer notes that certain of the sensations apparently arising in the intercostal spaces resemble muscle pain,¹ and that in large exudations where muscles and pleura are "much involved," the intercostal depressions are obliterated, so as to admit of deep pressure. He does not refer to these phenomena as indicating a period of relaxation in the muscle, although that seems to be the probable explanation.

In an editorial note Musser refers to a case in which pleurisy and intercostal neuralgia were concurrent. In the first week signs of pleurisy dominated; in the second, third, and fourth weeks intercostal neuralgia was most evident. An herpetic eruption developed along the course of the ninth intercostal nerve.

Rosenbach² refers to marked dyspnoea if there be much pain in the thoracic muscles, and speaks of rheumatic pains in these muscles as accompanying dry pleurisy. In common with other observers, he³ notes the respiratory asynchronism evinced by delayed excursion on the affected side. The chest deformity associated with contracting thorax, he says, may be due to degenerated and contracted muscles⁴ and the intercostal spaces may be obliterated, the ribs overlying each other like tiles on a roof.

The same writer⁵ is of the opinion that in affections of the thoracic muscles, such as rheumatism and intercostal neuralgia, contraction of the intercostal muscles may give rise to conditions that simulate dulness; at just this point it might be well to note that cedema, perivascular infiltration, and lipomatous change of the intercostal muscles would, theoretically, favor the same result. With full recognition of his entire unfittedness, it is not the writer's purpose to discuss the influence of the alteration in the intercostal tissues on physical signs, but any of the mentioned changes in the intercostal muscles would presumably influence the percussion note and probably modify the auscultatory sounds.

With regard to the pseudopleural friction sound, called by the French *bruit de cuir neuf*, Rosenbach⁶ accepts the condition as a muscle phenomenon, and it is not improbable that other pseudopleural friction sounds are, at least in part, of muscle origin. As will be shown later, pleurisy may be complicated with a myositis, and

¹ Diseases of the Bronchi, Lungs, and Pleura, Nothnagel's Encyclopedia, 1903, p. 845.

² Ibid., p. 849. ³ Ibid., p. 852. ⁴ Ibid., p. 853. ⁵ Ibid., p. 856. ⁶ Ibid., p. 864.

it would be of great interest to know if any friction sound results from movement in muscles the seat of inflammation. This could be determined, probably with great accuracy, by auscultation of muscles so situated as to exclude the probability of friction sounds arising from any other cause. It is well known that oedema of collagenous membranes, such as tendon sheaths, may give rise to friction sounds, and it is not impossible that the septal fibres or septal membrane between the external and internal intercostals, and possibly the movement of fibre sheaths or bundles, one upon another, might give rise to such friction.

Przewalski¹ calls attention to the narrowing of the intercostal spaces and increased resistance to intercostal digital pressure in all of 19 cases of pleurisy, 14 of which were serous and 5 suppurative. The sign is most easily elicited in children. He regards this narrowing of the intercostal spaces and fixation of the intercostal muscles as characteristic of pleurisy and analogous to *les attitudes fixes des membres* in inflammations of the joints. He does not seem to have suggested that the phenomenon he observed could have depended upon architectural change in the muscles of the area to which he draws special attention.

Although Rosenbach² speaks of extension by contiguity from pleura to peritoneum, the anatomical changes in the diaphragm accompanying such extension received no specific notice. The only study of the muscles of respiration in pneumonia and pleurisy with which I am familiar is that by Rohrer.³ This observer made a careful study of the diaphragm in pneumonia, pleurisy, and pericarditis, and shows that in pneumonia and pleurisy an interstitial myositis of the muscular portion of the diaphragm adjacent to the area involved, whether it be pleura, pericardium, or peritoneum, frequently results. His studies include only lesions of the muscle areas of the diaphragm; he makes no reference to any involvement of the tendon. His excellent paper is illustrated by a number of exceptionally good photomicrographs of the condition that he describes. This phrenitis or diaphragmitis, Rohrer believes, may

¹ Centralbl. f. Chir., 1902, vol. xxix. p. 377.

² Ibid., p. 330.

³ Maryland Medical Journal, September, 1902, No. 9, vol. lxv. p. 391.

result from (1) direct extension, (2) extension by the lymphatics, and (3), though rarely, hæmatogenous infection.

PERSONAL OBSERVATIONS. The writer has studied the intercostal muscles in 7 cases; 2 of these were croupous pneumonias with plastic pleurisies, the pneumococcus being isolated from the lung and pleural effusion. Two were tuberculous lesions of the pleura; one of them a direct extension of tuberculosis to the pleura from a large area of recent tuberculous pneumonia in the presence of a dense fibrous adhesion, irregular in outline, 12 cm. in length anteroposteriorly, and possessing a maximum breadth of 6 cm., situated immediately over and involving the lower portion of the upper lobe of the right lung; the anterior margin of the sclerotic area corresponding to the costocartilaginous junction. The other case was a frank tuberculous serofibrinous pleurisy, acute in time, the tubercle bacillus being demonstrable in films from the exudate, and the condition associated with a number of chronic tuberculous lesions of the lung, some of which were fibroid, partly encapsulated, others evidently more recent. Two other cases were acute pneumococcal pleurisies, one in a child (seven years), the other in an adult, and associated with pericarditis. The seventh case was a chronic empyema, for which Professor Keen performed an extensive resection of the thoracic wall.

In both cases of croupous pneumonia the diaphragm was also examined. One case showed the acute leukocytic infiltration similar to that described by Rohrer, with, at points, evident beginning abscess formation. This is evinced by areas of necrosis extending the breadth of six to eight muscle fibres, the necrotic detritus being richly infiltrated with polymorphonuclear and hyaline leukocytes. At such points, by appropriate staining methods, organisms possessing the morphology and tinctorial characters of the pneumococcus can readily be demonstrated. The change not mentioned by Rohrer, but clearly made out in this case, is an evident involvement of the lymphatic tracts of the tendon of the diaphragm. Sections of this tissue show irregular columns of leukocytes arranged parallel with the fibres and sometimes so solidly grouped as to constitute almost an injection of what appears to be a lymph vessel. Within the muscle area and occasionally in the tendon the fibrin content of the exudate can be demonstrated satisfactorily by Weigert's fibrin stain.

Fragmentation of the muscle fibres and the appearance within them of phagocytic leukocytes would indicate that an attempt was being made to clear up the areas of necrosis by the ordinary process for the removal of necrotic tissue. In this particular instance I have found no evidence of further effort at repair. The acuteness of the process probably explains this finding. The change in the muscle, so far as can be determined from the examination of a single specimen, is restricted to the side involved. In the tendon, however, the lesion is a little more diffuse. The diaphragm in the other case of pneumonia and also the intercostal muscles in the same case show practically no structural alteration, at least nothing that could not be attributed to such variation in spacing of fibres and in size as might be found in any muscle. The changes found in the other 5 cases may be grouped together with the case of acute tuberculous pleurisy. They were not marked. In another case the lesion is much more advanced, and later will be described in detail. In the two acute pneumococcal infections engrafted on catarrhal pneumonia, the lesions are evident and clearly recent; the one chronic case must be considered separately.

The number of cases examined is, of course, too small to determine with accuracy, and, to the satisfaction of the critical observer, the exact order in which the lesions occur. Probably the following order will require revision upon more extended observation; it is at present submitted more for the purpose of indicating the character of the lesions found than with the idea of definitely establishing the chronological order in which the processes occur:

1. Muscle fibres showing marked granular change, inadequate tingibility, and unsatisfactory stain reaction, such as commonly observed in granular tissues, can be recognized in all cases. It is not clear that this granular degeneration or cloudy swelling can be attributed to inflammation in the adjacent serosa, as it closely resembles, indeed, is probably identical with, the cloudy swelling observed in muscles as a result of infectious processes where apparently the toxin is acting through the blood. It would, therefore, seem wise to regard this change as a part of an alteration affecting the general musculature, the intercostals, in common with other muscles, manifesting their share in the change induced by the systemic action of toxic bodies.

2. With this alteration probably begin the changes that are incident to the involvement of and extension from the adjacent serosa. Muscle fibres are dissociated, the separation in some instances being quite distinct. The presence of a granular acidophilic deposit around the muscles and interfascicular connective tissue indicates that we are dealing with an œdema; but few leukocytes can be seen in this stage. The muscle cells stain poorly; the connective tissue does not respond with its wonted activity to the usual connective-tissue dyes. The component cells are swollen and granular, and occasionally a faint network of fibrin can be demonstrated at selected points. There is not, however, in this stage, any conspicuous addition of a fibrin-containing substance. With this condition, bands, groups, and bundles of muscle fibres may be seen showing a change that, so far as I can observe, cannot be differentiated from the hyaline, vitreous, or diaphanous degeneration described by Zenker, known to occur in the muscles of the abdominal wall in typhoid, and now recognized to be a much more widely distributed lesion often found in other conditions. In these hyaline areas muscle fibres often appear to coalesce, so that the hyaline change seems to include the interfascicular tissue as well as the muscle fibre. Whether this change be a secondary degeneration or necrosis, probably our present methods are inadequate to determine. That it is not identical with coagulation necrosis containing fibrin can easily be established by the absence of fibrin in some areas where the process now under consideration is conspicuous; we are familiar with processes clearly necrotic and closely resembling, if not identical with, the change now under consideration, that could not, with propriety, be grouped with the necroses. As this, however, is neither the time nor the place to enter into the academic discussion as to what constitutes necrosis and what degeneration, it does not seem necessary to consider further the change present, the appearance of which is fairly well reproduced in Fig. 1.

3. It seems reasonable to assume that the stage now to be described is preceded, at least in some instances, by the alterations mentioned above. The dissociation of the fibres, the granular material, the areas of hyaline change, can still be recognized, or at least appearances of their having been present may be more or less fully identified. In this stage there is a leukocytic infiltration of the muscle

similar to that shown in the photographs illustrating Rohrer's article. The leukocytes present in the specimen studied are mostly of the mononuclear type, many of them corresponding to the large lymphocyte or hyaline cell; the polymorphonuclears have not been exceedingly numerous; eosinophiles have not been identified in the altered areas. The dissociation, fragmentation, granularity, and necrosis of the muscle fibres are in this stage very much more evident. It is a diffuse process; some of the fibres appear to suffer to a marked degree, almost amounting to a necrosis, while others

FIG. 1.

Intercostal muscle, transverse section, from a case of epipneumonic pleurisy, showing area of necrosis. Tissue fixed in Zenker's fluid; hæmatoxylin and eosin stain. A, A. Necrotic area in some portions of which the shadowy outlines of muscle fibres may still be distinguished. B. A few mononuclear leukocytes, mostly of the lymphoid type, aggregated on the margin of the necrotic area. C, C. Fragmenting vacuolated fibres, of which several can be seen in the field.



but slightly altered may be seen immediately adjacent, in a way resembling very closely the myocardial degenerations that have been described in various infectious diseases. (See Fig. 2.) Fibrin is abundantly present; bacteria may be conspicuous, while in the preceding forms they were at most but scanty and usually absent. There is in this stage no difficulty in the identification of organisms that in the pneumonias and epipneumonic pleurisies may, with reasonable certainty, be considered pneumococci. Sometimes the bacteria are grouped in the spaces between the muscle fibres in such

a manner as to indicate dissemination along a lymph vessel, possibly only a larger lymph space.

It has not been possible to secure specimens showing what might be looked upon as the next stage, and as to the ultimate outcome, should the patient recover, it is not possible at the present time to offer any unassailable opinion. Evidence of abscess formation is usually absent; the process seems more diffuse, but one could easily appreciate that the small necrotic areas infiltrated by polymorpho-

FIG. 2.



Intercostal muscle, transverse section, from a case of epipneumonic pleurisy, showing dissociation of fibres, interfascicular leukocytic infiltration, and slight fibrin formation. Tissue fixed in Zenker's fluid; hæmatoxylin and eosin stain. A, A, A. Granular and fragmented muscle fibres B. Accumulation of leukocytes and fibrin around and extending between the muscle fibres. In some areas the change is more marked than in others, and at points many polymorphonuclear leukocytes can be seen.

nuclear leukocytes are really microscopic abscesses, such as can readily be demonstrated in the diaphragm. Our knowledge of the pathology of muscle inflammations leads us to infer that with the subsidence of active infection the necrotic muscle fibres would be removed by phagocytic cells (myoclasts); the interfascicular exudate would undergo absorption, and, with the formation of a certain amount of fibrous tissue, there would eventually result a moderate degree of muscle sclerosis. It therefore seems reasonable to

assume that where the disease lasts a sufficient length of time—where, in other words, the infection is permitted to continue—the changes between the stages just described and the conditions found in the specimen examined and reported below would fall under the head of subacute or chronic sclerosing myositis, which, toward the end, would give rise to the picture presented in the following case.

For the privilege of reporting this case I am under particular obligation to Professor Keen, who kindly placed at my disposal his notes and description of the operation, from which I summarize as follows:¹

F. A., male, aged twenty-two years. Admitted to the Jefferson Hospital on June 11, 1903. Patient of Dr. Boyer.

Left-sided pleurisy of six years' duration, terminating in empyema. Upon admission to the hospital the left side of the chest was fuller than the right. The intercostal spaces obliterated. Mediastinal organs displaced to the right. June 9, 1903, aspiration; three quarts of yellowish pus withdrawn. On June 16th Dr. Stewart excised two inches of the seventh rib on the left side at the anterior axillary line, opened the pleural cavity, evacuated a large quantity of greenish-yellow, turbid fluid, and inserted two drains. Bacteriological examination by Dr. Rosenberger at this time showed cultures of the micrococcus pyogenes aureus and albus. The urine contained albumin, hyaline and granular casts. Under drainage the patient improved and left the hospital on June 28th. Daily irrigation of the cavity was practised for some time before leaving the hospital. He was readmitted under Professor Keen's care on October 26th. The heart was still displaced somewhat to the right; the left side of the chest was still flat; diminished resonance over left lung, with respiratory sounds diminished in upper and absent in lower half of organ. Urine contained trace of albumin, but casts were not detected. Tubercle bacilli were not found in the discharge from the pleura. Pneumococci noted as absent. Staphylococcus pyogenes aureus still present, and an organism possessing the morphology and tinctorial characters of the diphtheria bacillus, but without pathogenic action for animals, was obtained in studies made by Dr. Rosenberger.

¹ The physical signs were characteristic and need not be detailed.

On November 4th Professor Keen again submitted the patient to operation, and the following record is from his notes:

"I made the usual large flap extending from the second rib, with a broad sweep under the arm down to the level of the seventh rib, and backward between the scapula and the spine. The entire thickness of the chest-wall, including a greatly thickened pleura, was then removed from the third to the seventh ribs, inclusive. The pericardium and pleura were exposed. I made no attempt at decor-tication, but only curetted the parts thoroughly, because the patient's condition was bad, with his heart pushing over to the right side, the left lung of very little use, and the right hampered by the displacement of the heart and the left lung; the operation was finished as rapidly as possible; after replacing the flap, which left a large opening at the lower portion, and packing some iodoform gauze to check the slight oozing, the wound was closed.

"On December 2d there were evidences of a beginning oedema of the lungs; he rapidly failed and died on the 4th."

No autopsy was obtained.

The specimen removed came to the laboratory for study and was submitted for examination to Dr. Ellis, Demonstrator of Morbid Histology, whose report is as follows:

"The specimen consists of a number of pieces of ribs varying from 2 cm. to 9 cm. in length, to which are attached masses of tissue; portions of this tissue are grayish in color, dense, and apparently fibrous. The surface of some of the masses is yellowish or yellowish-gray and shows areas of necrosis. Small fragments of muscle are also attached.

"The soft parts were fixed in Bensley's fluid, dehydrated, cleared, and infiltrated with paraffin. Sections were cut and stained by the usual laboratory methods.

"Microscopic examination shows the majority of the sections to be made up of fibrous tissue, most of which is in the early stages, though certain parts are quite dense. The margin of the sections bordering the most recent fibrous tissue is composed of embryonic and granulation tissues in which are numerous polymorphonuclear leukocytes. Beneath this formative zone is fibrous tissue in various stages of formation. Some of the sections contain considerable striated muscle, which has undergone pronounced changes. Certain

areas show a high degree of fatty infiltration, while in others this is associated with a marked increase of the fibrous tissue. The latter change is for the most part fairly recent in point of time. The muscle fibres show varying degrees of atrophy. Vacuolization and fragmentation of the fibres are also seen."

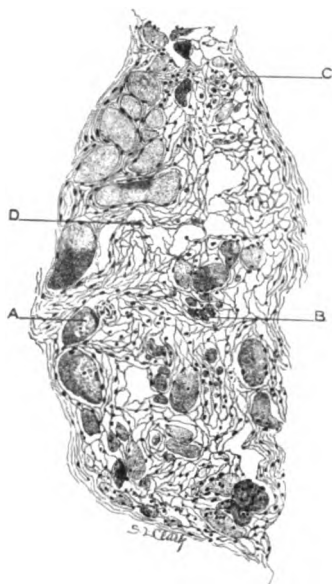
It will be observed that this specimen shows marked atrophy and advanced destruction of the muscle fibres, with intercalation of newly formed and forming fibrous tissue with, at points, advanced substitutive lipomatous infiltration. It seems reasonable to assume that the long-continued infection of the pleura has given rise to this alteration in the intercostal muscles. These structures in this specimen show no evidence of an existing infection. The process has assumed a very much more chronic type manifested by the development of formative tissue in the intramuscular septa and in the interfascicular spaces. Necrotic processes are no longer active in the muscles. Fig. 3 represents a small area from this specimen, and shows to advantage the essential changes in the muscular tissue.

PATHOGENESIS. It seems to the writer that the cause of these changes in the intercostal muscles is clear. Feiner has shown that after injecting fluids containing suspended granules into the pleura the extraneous matter may be demonstrated in the costal pleural lymphatics, and that but little resorption takes place through the pulmonary pleura. When we consider the fact that in inflammations of the lung and pleura the interlobular and intralobular lymphatic systems can be seen engorged with products of absorption from the lung principally, we can understand how the parietal or costal lymphatic system must necessarily care for the major part of the drainage from the pleural cavity. This being the case, toxic materials passing off by this route are brought in close proximity to the intercostal muscles and diaphragm; it seems reasonable to assume that direct lymphatic paths may become occluded, being in close proximity to the centres of irritation, and, therefore, collateral currents must form through the intercostal muscles, thereby exposing them to the dangers induced by more or less persistent bathing in toxic lymph. If the infection be active or the resistance low, or both, the pathogenic organisms may be carried into the muscle, giving rise to suppurative processes, such as have been described by Rohrer in the diaphragm, and figured in one of the preceding cases as occurring

in the intercostal muscles. If the bacteria be scanty or of indifferent activity or the patient's resistance high, they remain in the lung or pleura, and the muscles escaping direct infection suffer from the toxic action only.

Where the irritation extends over a considerable length of time and granulation tissue with its protective influence against infection clothes the costal pleura, or where newly formed collagenous tissue is intercalated between the muscle and the altered serosa, then

FIG. 3.



Intercostal muscle, transverse section, from a case of suppurative pleurisy of several months duration, showing advanced fibrosis and lipomatous change. Tissue fixed in Zenker's fluid; hæmatoxylin and eosin stain. A. One of several granular fibres, some of which are fragmented and undergoing absorption. B. A small group of greatly shrunken muscle fibres. C. Relatively large mononuclear cell, not very abundant but commonly associated with fibroblastic elements. D. The leader from this letter passes between two imperfectly preserved fat bodies, a number of which are present in the newly forming or formed fibrous tissue. The fat content is scanty in the particular field from which this drawing is made.

products reaching the muscle would probably be less active or materially modified toxins without evident bacteria. Here, then, results the chronic sclerosing change comparable to that seen in the muscles adjacent to tuberculous areas elsewhere in the body, as, for example, around tuberculosis of the hip, vertebræ, etc. In the more acute stages of the process the degenerative and necrotic change seen in the muscles may be attributed to the action of the toxins, passing through the lymphatics of the muscles or diffusing into the

muscle tissue. In the later acute cases bacteria themselves enter. In the cases of longer duration there might occur a chronic suppurative interstitial and parenchymatous myositis, but probably the patient would not survive an infection of this type, except purely as a local manifestation. The chronic alteration of importance is the sclerosing process by which the muscle is in part or almost wholly replaced by newly formed fibrous tissue in which fatty infiltration or lipomatous substitution almost constantly occurs.

The influence of the changes already described on the thoracic wall so fully suggest themselves that a detailed consideration need hardly be given. The clinician will at once think of the modifications in physical signs—muffling and alteration in auscultatory sounds depending upon increased density of the thoracic wall—brought about by any of the changes described, including serous infiltration, cellular accumulation, as well as fibrous and lipomatous change in the intercostal muscles; the influence of the change upon the function of these muscles will also be apparent. Even slight myositis is associated with rigidity, a more or less successful attempt at fixation, and this fully accords with the recognized clinical data.

A large amount of space might profitably be devoted to consideration of the influence of the change upon respiration, but as this is evident, I need but touch upon this point. Hamberger's observations on the functions of the intercostal muscles in respiration has received general acceptance, and has been corroborated by the studies of Newell Martin and Hartwell, Masoin, and R. du Bois-Reymond.¹ The fact that the internal muscles are actively operative in respiration only when the function is labored renders more important the alterations now under consideration, because with alterations in the diaphragm, the principal muscle of respiration, and with the influence of intoxication upon the respiratory centres, and satisfactory evidence of narrowing of the intercostal spaces, as suggested by Przewalski, it becomes at once clear that structural alterations in these muscles must materially influence the alterations in chest volume upon which air intake so largely depends. The fact that the external intercostal muscles are but slightly involved and often

¹ The details of muscular action in respiration are fully considered by Starling in Schäfer's *Text-book of Physiology*, vol. ii. pp. 274-280; he also cites the authorities to whom I refer.

escape does not modify this observation, because physiologists are fully familiar with the fact that opposing muscles are reciprocally influenced. Mention should be made of the influence of sclerosing myositis in the production of costal fixation in the chronic cases; whatever views may be entertained with regard to the inexpandibility of lungs long atelectatic, the condition of the ribs as regards motility cannot be ignored. The fixation of the affected side in acute cases may be, as is usually held, reflex, but it may also depend upon the spastic fixation of muscles (intercostal and diaphragmatic), the seat of pronounced architectural change.

Structural alterations in the intercostal muscles possibly clear up to some extent the observations that intercostal rheumatism, intercostal neuralgia, etc., are complicating or associated phenomena of pneumonia and pleurisy. In this connection there are several factors in this field that the writer appreciates are not worked out. Probably the most conspicuous is alteration of the nerves. Some of the sections show nerves that appear oedematous. In none of them has any cellular infiltration been observed. The tissues have not been prepared suitably for the demonstration of myelin degeneration, and this question must be taken up with some detail later. I might at this point, however, say that sections show, what histologists so far as I know do not mention, namely, that nerve filaments or even relatively large trunks can be seen coursing between the internal intercostal muscles and the adjacent pleura. They are so situated as to expose them to all the toxic substances permeating the adjacent muscle. In one block of tissue from an acute case two relatively large nerve bundles can be seen immediately below the serosa imbedded in a small cushion of fat; the epineurium touches the serosa, and a vessel lying in immediate proximity contains, on transverse section, seventeen erythrocytes, two polymorphonuclear leukocytes, and one hyaline cell—presumably a local leukocytosis. The nerve bundle is retracted from its sheath, on the inner aspect of which can be recognized transverse sections of two capillaries containing red cells, but no leukocytes; there is no leukocytic infiltration of the sheath or nerve. Another specimen contains a longitudinal section of a nerve that at one point shows a suggestion of cellular infiltration and contains a widely dilated capillary. Such axis-cylinder stains as have been applicable to Zenker material demonstrate no noteworthy

change in the myelin sheaths and axis-cylinders of the nerves, but, as usual in such material, myelin stains have proved unsatisfactory.

The foregoing offers no sufficient anatomical basis for the conclusion that the nerves suffer; nevertheless, I am satisfied that in such instances as the one narrated they cannot long escape. Their perilous situation exposes them to the noxious influences of infection, toxic bodies, and other coincidents of inflammation, to the action of which nerve elements are conspicuously susceptible. It would be interesting to know if the clinicians have observed any paralytic phenomena that indicate a toxic degeneration or neuritis involving the phrenic nerve or motor branches to the intercostal muscles. Alteration in the sensory fibres is strongly indicated by certain of the clinical factors; will the clinicians kindly advise us what, if any, symptoms or physical signs point to motor involvement? I feel reasonably certain that there is no sufficient reason why the motor nerves should escape.

An extremely important point to be determined is whether there are any lymphatic ways corresponding to intercostal spaces in which this change is most marked. While I have no information that would justify a positive conclusion upon this point, the fact that well-marked changes may be seen in one area of an intercostal muscle, and the block of tissue from an adjacent neighborhood fails to show the alteration, leads to the belief that the lymphatic course or tract should merit special consideration, and it appears that in a very general way only have the anatomists and histologists solved this problem. Possibly we have, in what might be called pathological injection of the lymphatic spaces and vessels, an important adjuvant in the study of the lymph courses. I have had no opportunity to study the changes in the lymph trunks draining the costal pleura; such a study, based upon experimentally produced inflammations of the lung and pleura, is needed.

An important question suggested by Dr. Riesman is what would the intercostal muscles of the sound side show? In one of the cases of pneumococcal pleurisy the muscles of the other side escaped, or at least showed no structural change. I am not inclined to believe that the opposite side is involved, unless thrombosis of the costal lymphatics of one side might lead to an anastomotic current passing

to the other; such spanning of the mediastinum would seem improbable.

Another point upon which these studies are inadequate is the frequency with which the intercostal involvement occurs. Five of the seven cases studied are Philadelphia Hospital patients, and those familiar with the Blockley morgue know that we may draw incorrect conclusions as to the frequency of concurrent conditions, because we are dealing with a class in whom coincidence of pathological processes is a conspicuous feature.

Kuettner¹ has made an exhaustive study of the perforating lymphatics of the diaphragm. He shows that the drainage territories of the diaphragm are such that abundant opportunity is afforded for transdiaphragmatic infection, and has so worked out the lymph paths as to show that while each half of the organ possesses its own lymphatic field communicating with other parts by way of lymph nodes only, all parts of the diaphragm possess anastomotic communication with the pleura and peritoneum. The anterior and posterior lymph vessels communicate and drain in common into certain glands; some of these vessels vertically transverse the diaphragm twice in coursing over it. Taken with the studies of Rohrer and my own observations, it seems that Kuettner's work forms the necessary link in completing our already fairly full comprehension of the possibilities of transdiaphragmatic infections. That a juxtaposed abdominal viscus may infect the pleura or pericardium (*e. g.*, hepatic, splenic, and perirenal abscesses and gastric ulcer) has long been common property, but that lesions of a finer texture may be recognized, and that the four great serous cavities are really intercommunicating lymph spaces, is within recent times leading to deductions some of which may be important. Is it possible that the pneumococcal inflammations of the peritoneum (even when primary) may be transdiaphragmatic infections, the lung and pleura escaping in some cases? The frequency with which the ribs suffer typhoidal osteomyelitis is suggestive, and if, as Fraenkel holds, the typhoidal spondylitis is really a bacillary infection of the cancellous tissues of the bodies of the vertebræ, the demonstration of abdominal and thoracic lymph systems as so closely allied threatens,

¹ Thirty-third Congress of the German Surgical Society, June, 1903; *Centralbl. f. Chir.*, 1903, No. 36; *Beiträge z. klin. Chir.*, Tübingen, vol. xI., No. 1.

as the result of a minor disclosure, to lead one into a labyrinth of unjustified speculation.

It is not the purpose of this paper to consider transdiaphragmatic infections, the passage of fat-necrosing substances through the diaphragm, and cancerous extension from peritoneum to pleura, or the reverse; these subjects have recently been studied by von Brunn¹ and Jensen,² in pneumococcal peritonitis; by Henle,³ in an article on "Pneumonia and Laparotomy;" by Truhart,⁴ in considering intrathoracic fat-necrosis in disease of the pancreas, and by Tilger,⁵ in pleurisy and peritonitis; Kuettner⁶ discusses and gives most of the references. The demonstration of lesions in the tendon of the diaphragm is only a minor extension of Rohrer's observation.

In conclusion, I wish to express my appreciation of the kindness of Professor Keen, and Drs. Rosenberger, Ellis, and Funke, for helpful aid in the preparation of material upon which this paper is based.

¹ *Beiträge z. klin. Chir.*, Bd. xxxix., Heft 1, p. 94.

² *Langenbeck's Archiv*, Bd. lxx., Heft 1, p. 95.

³ *Ibid.*, Bd. lxiv., Heft 2.

⁴ *Pankreas Pathologie*, 1902.

⁵ *Virchow's Arch.*, Bd. cxxxviii. p. 499.

⁶ *Loc. cit.*

A REVIEW OF LITERATURE RELATING TO SERUM DIAGNOSIS.*

BY

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It is not my purpose to attempt an exhaustive review of all the literature bearing upon this interesting subject, but to include, so far as possible, the most recent progress in serum diagnosis.

As is well known, the first application of serum reaction to diagnosis was in enteric fever. Ross claims that the discovery should be accredited to Grünbaum who, in 1896, while working in Gruber's laboratory, in Vienna, obtained positive agglutinative reactions in typhoid fever. The first test was made on March 14. This discovery was promptly corroborated and quickly followed by other investigators obtaining agglutinative reactions in other diseases and with other bacteria. As examples of the widespread application of the test, the following organisms are now agglutinated by the serum in their selective cases: *Streptococcus pyogenes*, diplococcus of pneumonia, bacillus of plague, colon bacillus, bacillus of dysentery (Shiga), paratyphoid bacillus, paracolon bacillus, Gärtner's bacillus, Booker's bacilli, staphylococci, gonococcus, spirilli of cholera and of relapsing fever, bacillus of tuberculosis, members of the proteus group, bacillus of tetanus, *Oidium lactis*, bacillus of diphtheria, and others. Not only are bacteria subject to this reaction, but animal parasites, as the trypanosomes, have been agglutinated by the serum of patients suffering from sleeping sickness and trypanosomiasis fever.

Freyer¹ claims that the blood of all native Indians possesses agglutinating power in health, but this statement is contradicted by W. C. Brown,² who made a number of tests with negative results.

* Read before the Pathological Society of Philadelphia, February 11, 1904.

Technic.—The technic of the Widal test is perfectly simple, and usually consists in bringing together the bacilli in young bouillon culture, or a water suspension from an agar culture, and the serum of the individual in a proper dilution. The culture should not be over 24 hours old, and the bacilli actively motile, although dead typhoid bacilli may also be used for the reaction. Examine the culture before beginning the test, to see that clumps are not present. If they exist, the culture should be filtered through paper and the filtrate used for the test. The blood or serum may be collected in various ways: (1) By a capillary pipet in which coagulation and separation occur; (2) by the white blood cell pipet in which a dilution of 1 to 20 is made; (3) obtain pure serum from a blister; (4) dried blood may be used.

The technic employed at the Jefferson Hospital and Philadelphia Hospital is the use of a nonincubated bouillon culture of the typhoid bacillus not over 24 hours old, mixing 1 drop of this culture with 1 drop of diluted blood. The dilution of the blood, 1 to 20, is facilitated by means of the pipet used for counting leukocytes; using a drop of each, a dilution of 1 to 40 is obtained; 30 minutes is given as the time limit.

Haedke³ recommends the mixture of a loop of solid culture with typhoid serum on a glass slide. McWeeney,⁴ by mixing 1% serum in a hanging drop with bouillon culture, and placing in the incubator at 37° C. for 4 hours; twisted and convoluted chains of motionless bacilli will form if the case is one of enteric fever.

When a test is made with dried blood, it must be moistened with distilled water, the difficulty of obtaining an accurate dilution being one objection to this method. There is much difference of opinion as to just how much the serum should be diluted. Most observers recommend a dilution of 1 to 20, or 1 to 40; some use 1 to 200, and even 1 to 20,000 has been found effective in an occasional case. It has been found very often that the reaction is negative with dilution of 1 to 20, and positive with dilution of 1 to 50, and *vice versa*. This apparently is accounted for by the presence of certain bodies—proagglutinoids, described by Shiga⁵—that develop from the agglutinins and combine with the bacilli, but lose the power of combining with the agglutinin. These bodies—proagglutinoids—are developed from the agglutinins through extraneous influences, and possess a greater affinity for the bacilli than the unchanged agglutinins, having lost their agglutinophore group, but

retaining the haptophore group; they have been produced artificially by heating dysentery-immune serum to 60° C., or by shaking with chloroform, or exposing it to sunlight for a few days (Eisenberg and Bail). Coleman and Buxton⁶ insist upon a dilution of 1 to 50.

J. S. Billings, Jr., uses a dilution of 1 to 20; clumping and death of the bacilli must occur in 10 minutes.

Bryant⁷ says that in Guy's Hospital it is customary to use 50%, 5%, and 0.5% dilution and Widal's reaction is not considered positive unless clumping and immobility of the bacilli occur with the 1 to 200 dilution within half an hour. Examinations made before the eleventh day of the disease with a negative result are of little value. In this connection he mentions W. C. C. Pake's analysis of 304 consecutive cases, in which the error was only 3.03%.

Baltharde⁸ states that by the injection of nonfatal doses of the typhoid toxin an antityphoid serum possessing agglutinating power of 1 to 100,000 but without decided bactericidal action (*in vitro*) may be obtained.

Libman⁹ claims that if the blood is employed immediately after drying, the result is not so good as when it is used some hours later. However, in the summer, if the blood is not taken for the test within 24 hours, it is not so easy to obtain the Widal reaction.

Ficker¹⁰ has perfected a fluid to which he has applied the name diagnosticum, with which it is possible to obtain the Widal reaction without the necessity of living cultures of typhoid bacilli. The fluid is sterile, slightly turbid, and is said to keep well for 9 months. The reaction is perceptible to the naked eye, absolutely unmistakable, and occurs at ordinary room temperature. "The fluid is derived once from one and the same typhoid stem."

A. J. Wolff¹¹ recommends smearing an agar slant with typhoid feces and from the growth resulting, inoculating 1 or 2 tubes of bouillon. The bouillon must

react from 1% to 2% alkaline with $\frac{N}{10}$ acid, using phenolphthalein as indicator. A sample of the blood is taken and mixed with the bouillon culture and placed under the microscope. If there is sufficient agglutinative material present, the typhoid bacilli will clump while the colon bacilli remain active. In 35 tests thus made, every case that gave a positive reaction by this method proved to be typhoid fever.

Proeschner¹² recommends collecting the blood in U-shaped tubes of a diameter of 2 mm. The tubes are closed, centrifugalized, and the serum separated by breaking the tube with a file. The serum is then transferred by capillarity from the tubes to pipets graduated in 0.01 cc. This is then diluted in 1 to 10 normal salt solution, and portions are placed in small test-tubes, the first part without additional dilution, the second diluted one-half, and so on through 5 dilutions. Each tube then receives 5 cc. of typhoid bouillon culture, which, after 24 hours' growth, has been killed by adding 1% formalin. This diluted culture is then added to the tube, in quantity equal to that which the tubes already contain. The tubes are at once emptied into small glass dishes and placed in the incubator for 1 to 2 hours. After this they are examined with relatively low powers (about 50 diameters) when the agglutinative masses can readily be seen.

The reaction occurs, by the methods just given, in from 15 minutes to 2 hours; while in the macroscopic test in which a small tube of the culture has added to it blood or serum from the patient, 5 or 6 hours is necessary for the reaction to be completed.

In the microscopic test a positive reaction is said to occur when all the organisms in the field, group or agglutinate and motility ceases. In the macroscopic or tube test a positive reaction is said to occur when the uniform turbidity clears and the bacteria settle in small masses at the bottom of the tube.

A. E. Wright,¹³ in the case of patients suffering from or preventively inoculated against tuberculosis, uses a suspension of extremely fine detritus of tubercle bacilli in carbolized water. By employing 1 to 1,000 solution of common salt to dilute the serum, instead of 8.5 per 1,000 solution prescribed by Koch, fallacious agglutinations and precipitations are completely avoided.

Wright's modification of Koch's procedure is as follows:

A minute quantity of powdered tubercle bacilli is placed in an agate mortar, to which is added, drop by drop, a 0.5% solution of carbolic acid. After triturating for a few minutes the turbid suspension is siphoned into a capsule. After sealing the ends of the capsule it is centrifugalized and the supernatant milky fluid, which separates in a few minutes, is used for the test. The blood is obtained in a special capsule, which is then placed in a centrifuge until the serum separates from the cellular elements. A capillary pipet is then used, and into this is aspirated one volume of the undiluted serum, and one volume of the test fluid described before. This mixture is

expelled, and after thoroughly mixing upon an ordinary microscopic slide, exactly one volume is reaspirated into the stem of the pipet.

Having divided off with a suitable bubble of air, there is introduced into the stem of the pipet one volume each of serum and of the inert diluent (1 to 1,000 solution of sodium chlorid). These two last mentioned volumes are again expelled, and after mixing, constitute the quantity of diluted serum for our second test dilution. Having mixed this on a slide the mixture is again reaspirated, and as in the former case and all subsequent dilutions, using exactly one volume of the mixed fluids. Another serum dilution is now made, employing for this purpose a full volume each of two-fold dilution of serum and of the inert diluent. We then fill upon these principles in succession (into the stem of our pipet) a series, ordinarily 7 or 8 graduated dilutions of serum mixed in each case with a precisely equivalent volume of the bacterial suspension. Completion of the series is reached by introducing into the pipet a mixture of equal volumes of the inert diluent and test fluid to serve as a control. The pipets are then sealed and placed upright in the incubator or on the laboratory bench. After an interval of 12 hours, flocculation and deposition associated with a corresponding clearing of the supernatant fluid takes place. The precipitate in the two-fold dilution is in most cases—presumably as a consequence of bacteriolysis—markedly less in bulk than the precipitate in the succeeding dilution. After standing for a long time, a deposit makes its appearance also in the higher dilutions of the serum and in the control.

Besides tuberculosis, this method is also useful in those suffering from or preventively inoculated against typhoid and Malta fevers.

Romberg¹⁴ recommends mixing a dry culture of tubercle bacilli with 1 liter of bouillon containing 5 grams of carbolic acid. For use 1 part of this is mixed with 3 parts of distilled water. One part of serum extracted by wet cups is added to 5, 10, 15, or 20 of the emulsion which is left in the tubes. If at the end of 24 hours this becomes clear, the reaction is considered positive. The test is not entirely reliable.

Koppen¹⁵ treats the tubercle bacilli with caustic potash solution, thus saponifying them. The stem fluid which he uses for the agglutination test is milky, and homogeneous, and does not become putrid. After this saponification the tubercle bacilli take the stain as readily as before.

Thellung¹⁶ finds that agglutinins can be produced by the injection of tuberculin into guineapigs and rabbits. It is also claimed that the agglutination does not occur constantly or regularly in tuberculosis.

Lagriffoul,¹⁷ in the serum diagnosis of tuberculosis, adopts the technic of Arloing and Courmont. The cultures are made in a 2% peptone medium containing 6% glycerin. This medium is reinoculated every 20

days and incubated at 30° C. with agitation once daily. Macroscopically the test was facilitated with dilutions of 1 to 5, 1 to 10, and 1 to 15.

Loeb¹⁸ uses an 8 to 12-day old culture of the tubercle bacillus previously grown on potato and homogenized. To this is added clear blood-serum or serous effusion in the proportion of 1 to 5 or more. This is followed if the reaction is positive by a flocculent precipitate in the course of 6 hours.

Neufeld¹⁹ studied the agglutinative action of the serum of immunized animals on cultures of the pneumococcus in broth by the usual methods and was thus the first to note typical agglutination reactions in various dilutions, both microscopically and macroscopically. In dilutions of 1 to 50 he was able to obtain the reaction in from 15 to 30 minutes.

Bezancon and Griffon²⁰ inoculated 1 cc. to 2 cc. of clear undiluted serum with pneumococci and observed the appearance of the growth, at the end of 15 or 16 hours' incubation, to be characterized by the formation of a membrane at the bottom of the tube. This membrane consisted of branches and chains of pneumococci; this so-called agglutination can be observed by the unaided eye. These two observers then applied the method to 186 patients, among these being 64 of undoubted pneumococcus infection. In the serum from these patients the growth in bunches and chains was observed easily and constantly. The dilutions used were 1 to 50; they found that the results were very uncertain.

Weaver²¹ in testing the agglutination reaction in scarlet fever patients and others, used cultures of the streptococcus in bouillon which was neutral to litmus and 1% acid phenolphthalein. The blood was obtained from a vein of the arm and serum allowed to separate from the clot in an icebox. The serum was diluted with the same bouillon as used for the culture in strengths of 0.5, 0.25, and 0.125; by means of pipets of uniform size, one part of these various strengths was added to 30 parts of the 24-hours' bouillon culture. The mixtures of serum and culture were then placed in small test-tubes each containing about 1 cc. kept at room temperature and examined. If a positive agglutination reaction took place, a sediment formed at the bottom of the tube made up of flakes and granules, which would not break up upon agitation. The agglutination takes place more rapidly in the incubator than at room temperature, often being complete in 1 hour and usually in 3 to 5

hours ; at ordinary room temperature agglutination took place in 18 to 24 hours.

Wadsworth," in the agglutination tests in cases of pneumococcus infection in man and animals, uses a peptone broth made from meat infusion, which has been carefully neutralized before boiling. In a flask containing 200 cc. of this medium, the maximum growth of the pneumococcus was evident in 24 or 36 hours. At this stage the culture was centrifugalized, the clear fluid decanted, and the sediment shaken with about 15 cc. of isotonic (0.85%) salt solution. This left a dense, finely divided suspension of pneumococci, less than 48 hours old. Dilutions, with the serums to be studied, were then made in small, slender tubes and observed for some 12 to 18 hours at 37° C. The more marked reactions may be complete in 5 or 6 hours or less, but 12 or more hours are often required to bring out the more delicate tests. Serums stored in the icebox were found to be active for 4 or more months; the lytic power was gone, and the agglutination did not appear in high dilution; but in low dilutions immediate and complete reactions took place.

The normal serum of the rabbit always failed to agglutinate the pneumococcus cells. This was also the case with the serum of the cat and dog. Normal bullock's serum, however, gave some very marked agglutinations, even in dilutions of 1 to 50. Ascitic fluids tested also failed to agglutinate in dilutions of 1 to 5, and 1 to 15, but normal serums (human) gave reactions in dilution up to 1 to 10 in less than 18 hours; 1 to 30 failed to agglutinate. In 3 cases of lobar pneumonia positive reactions were obtained in dilutions of 1 to 10 after 5 hours' incubation.

Cairns " insists upon a perfectly homogeneous culture of *Bacillus pestis* for the serum diagnosis of the disease. For the reaction he uses a small test-tube 9 cm. in length and 0.7 cm. internal diameter, into which a drop of the blood-serum (collected in a small Pasteur pipet) is placed, and then the culture of the organism, up to the required dilution. The cultures are prepared by taking a 24 or 36-hour incubated growth upon agar, and filling with 0.75% sterilized salt solution to cover the solid medium. The growth is then as far as possible transferred to the salt solution by rubbing the surface of the agar with the blunt end of a Pasteur pipet. These emulsions are then set aside in a sterile test-tube for a short time, to allow any cohering masses to settle. A

too concentrated emulsion is agglutinated very slowly and often very imperfectly; while the exact degree of dilution is undoubtedly a matter of some importance, it can only be determined after considerable experience in agglutinative work. The tubes are then set aside and when complete sedimentation occurs—18 to 24 hours—a positive reaction is recorded.

Klein,²⁴ in preparing a homogeneous culture of *Bacillus pestis* for the agglutinative reaction, used a gelatin culture distributed in a 0.75% physiologic salt solution. His reason for using a gelatin culture is that, in his opinion, the surface colonies upon this medium are less viscid and drier than those upon agar. "If to a good salt emulsion of plague bacilli—taken from the gelatin surface—bouillon is added in the proportion of 1 of bouillon to 20 of emulsion, the result of positive agglutination is evident in from 12 to 15 minutes." Experiments were then made with blood of rats that had been injected first with Haffkine's prophylactic, then with small doses and finally larger doses of living plague organisms. Klein found that in several animals thus treated, 3 and 5 weeks after recovery, agglutination took place in dilutions of 1 to 20, and 1 to 40, in 10 minutes.

McFadyean²⁵ showed that serum from horses with glanders possessed the power of agglutinating glanders bacilli. In the great majority of cases of glanders a 1 to 50 dilution of the serum produces marked agglutination in a few minutes, while in that of nonglandered animals no effect is produced under these conditions. He finds that a more delicate and reliable method is to grow the bacillus in bouillon containing a small proportion of the serum to be tested. In this way he has obtained a distinct sedimenting action with a serum, which did not agglutinate at all distinctly in the ordinary method.

Heanley,²⁶ in testing the sedimentation and agglutination reaction in cases of glanders, used one part of glanders serum diluted with 109 parts of normal salt solution, and 110 parts of emulsion of glanders bacilli in normal salt solution. The same procedure was adopted with 2 samples of serum from diphtheria patients. When examined in 10 hours the glanders specimen showed definite sedimentation, the others did not. A repetition of the experiment gave the same result, and a dilution of 1 in 505 also proved positive; typhoid and normal serum showed no sedimentation.

The glanders serum could be differentiated from the

others in about 4 hours, but the reaction became more obvious later. Eleven tubes containing blood were numbered, and included blood from 1 normal person, 2 from enteric fever patients, 2 patients with scarlet fever, 2 with glanders, 1 with tuberculosis, 1 with scarlet fever and diphtheria, and 2 patients with diphtheria. Dilutions of 1 in 505 were made and only the 2 glanders specimens gave the reaction. In another experiment samples of blood from 2 patients with enteric fever, 2 with scarlet fever, 2 with diphtheria, 2 with variola, 2 with glanders, and 2 specimens of normal blood were examined in dilutions of 1 in 220, and 4 tubes showed sedimentation. Dilutions of 1 in 505 were then made, and all showed sedimentation. These 4 cases included 2 cases of glanders, 1 of variola, and 1 of scarlet fever. With dilutions of 1 in 2,500 sedimentation was produced only in the glanders cases. In the microscopic agglutination test an emulsion of bacilli was made from a growth on sloped glycerin agar by half filling the tube with previously boiled salt solution and gently agitating for a few minutes. In one series of observations, a 36-hour culture was used and the serums and emulsion were mixed on a slide and covered by a cover-glass. Serum from a patient with glanders of 6 months' duration was diluted with 9 times its volume of normal salt solution, and then 10 of bacterial emulsion was added, making a dilution of 1 in 20. Serums from 2 patients with diphtheria were treated in the same way. It was found that in mixtures containing the serum of the diphtheria patients, clumping was marked, while in the preparation containing the glanders serum more bacilli were free than clumped. In using diphtheria antitoxin as the diluent of cultures, clumps were also quickly and completely formed.

Typhoid.—In typhoid fever the reaction sometimes is absent throughout, and this may be due to a too high dilution, therefore, a low dilution, 1 to 20, or 1 to 10 in some cases, should be used. Curschmann²⁷ claims that the reaction takes place only in the minority of cases before the termination of the first week; most frequently not until the second week, while rarely it is delayed beyond that time. Complete absence of the reaction is one of the rarest exceptions. Kennedy²⁸ claims that Widal's reaction may be present as early as the fourth day and may be continuously or intermittently present throughout the disease, or in unfavorable cases it may be absent altogether in the first few days. To obtain the

full value of the reaction, tri-daily tests should be made throughout the disease.

In 165 cases of enteric fever, Libman²⁹ obtained a positive reaction with 1 to 20, and 1 to 50 dilutions in 127 cases. In some instances as many as 16 days elapsed before the reaction was positive in 1 to 50, and in 8 cases that were positive in 1 to 20, there was no reaction in a dilution of 1 to 50. He claims that it is essential in performing the test that at least two dilutions should be made—1 to 20 and 1 to 50.

Cabot,³⁰ in a collated series comprising 5,978 cases of enteric fever, has found that a positive reaction occurred in 5,814 or 97.2%, while in 5,668 control cases, a positive reaction occurred in 323 or 5%. Gwyn and Block, in 151 cases of enteric fever, obtained a positive reaction in 144. In 4 cases it developed on the twenty-second, twenty-sixth, thirty-fifth, and forty-second days respectively. In only 26 cases was the reaction present before the seventh day of the disease. Stengel and Kneass,³¹ in 2,392 collated cases of enteric fever, found that a positive reaction was obtained in 2,283, and negative in 109 cases. Coleman and Buxton³² state that Brill finds that of 4,879 cases of typhoid, the Widal reaction occurred in 4,781, or 97.9%. The reaction is absent in paracolon infection.

S. S. Adams³³ reports that of 70 cases of enteric fever in which the Widal test was made, 50 gave positive reactions. Widal³⁴ states that the agglutination reaction fails in 1 case out of every 40 of enteric fever. He has seen it as early as the third day. The most reliable results are obtained during the second week. It may be positive in dilution of 1 to 8,000.

Allaria and Bozzolo³⁵ show that *Bacillus typhosus* may be recovered from the spleen and other organs of the newborn at autopsy, when before death the Widal reaction was negative. In 4 out of 11 cases a positive reaction was obtained at varying days following birth. In 2 cases placental blood gave a positive, and the blood of the newborn a negative reaction.

J. S. Billings,³⁶ in 1,908 specimens of blood examined during 1901 by the Board of Health, found that 304 showed a positive reaction, and 111 cases were considered typhoid clinically, although the blood was doubtful or negative. In 131 cases in which the reaction was doubtful, and in 1,362 in which it was negative, the cases proved not to be typhoid. In a large number of the positive cases the reaction was not obtained until the

seventh or eighth day. In a comparatively large number several examinations were made with negative results, and yet the autopsy showed the correctness of the clinical diagnosis. It, therefore, follows that although a positive reaction may be taken as meaning typhoid with almost absolute certainty, yet a negative result does not by any means preclude the possibility of typhoid, and demands that another specimen be sent if the clinical signs persist.

Libman,³⁷ in 3,514 tests in 816 cases, comes to the conclusion that the Widal reaction, when positive, always means the presence or preexistence of typhoid. Partial reaction should be negative, and a negative reaction does not exclude the existence of typhoid. Wilson,³⁸ in a study covering 1,650 blood-examinations for the Widal reaction, states that less than 7% are what might be called partial or incomplete. They occur with much greater frequency in tuberculosis and malaria than in typhoid. Wright and Semple³⁹ report 18 cases of enteric fever in which, after subcutaneous injections of 1 cc. of sterilized cultures of *Bacillus typhosus*, the blood of the patients caused arrest of motility and agglutination of bacilli as seen in Widal's reaction.

McFarland and Anders,⁴⁰ in reporting 230 cases of enteric fever, obtained positive reactions in 219, or 95.64%. Of these 219 cases, 128 showed the reaction before the eighth day, 36 during the second week, 45 between the seventeenth and twenty-first days, 8 not until the twenty-fifth day, and 2 as late as the twenty-eighth day.

Vickery⁴¹ obtained a positive Widal reaction in 41 out of 49 cases of enteric fever. Sears,⁴² in 203 cases of typhoid fever, obtained the Widal reaction in 168, and negative results in 33. Ruediger⁴³ in 30 cases of enteric fever, obtained a positive Widal reaction in 26 cases.

Elsberg,⁴⁴ in 36 cases of enteric fever, found the reaction present in 8 cases one month after convalescence. Hektoen,⁴⁵ in 2 cases of typhoid fever that were at first confounded with scarlet fever, obtained pure cultures of the typhoid bacillus from the blood, which in each case was agglutinated by the serum of the patient. Thacher⁴⁶ cites an observer who had applied the Widal test in 334 cases. He found it present in only 6% at the end of the first week, in 36% at the end of the second week, 67% at the end of the third week, and 94% on the thirtieth day. Dun⁴⁷ reports a case of typhoid fatal on the thirteenth day. The Widal reaction was absent on the

eleventh and twelfth days. He mentions that Wright (Glasgow) has observed that in severe cases the reaction is frequently absent.

Haim,⁴⁸ in a case of typhoid fever, isolated from the stools *Bacillus proteus vulgaris* which was agglutinated by the serum of the patient in dilution of 1 to 50. Widal's reaction was also positive in dilution of 1 to 50.

Harrington,⁴⁹ during an epidemic of typhoid fever, found that of 90 cases in which the Widal test was performed, 58 were positive, 25 negative, and 7 unsatisfactory for "various reasons." In some of these, 2 or 3 examinations were necessary before a positive reaction was obtained.

Pallard⁵⁰ has shown that in typhoid spine (*spondylitis typhosæ* of Quinke, 1899) the Widal reaction becomes more marked and increases with the augmentation of the spinal symptoms. He concludes that the condition is an osteomyelitis due to the Eberth bacillus.

Carr and Roughton⁵¹ report a case of sapremia in which, in the first days of the disease, a positive Widal reaction was obtained, but after 6 weeks failed to give the reaction.

The writer contributes 184 cases of enteric fever, of which 109 gave positive, and 25 negative reactions. In 153 cases other than enteric fever, a positive reaction was obtained in 4 cases each of influenza and pleurisy, 1 each of malaria, peritonitis, parotitis, and pneumonia. A number of cases of typhoid fever in which a negative reaction was obtained, were diagnosed as "abortive typhoid."

Browne and Crompton⁵² state that Widal, in the examination of 40 cases of typhoid, found 11 that gave the reaction long after convalescence. One reacted 8½ years after with a dilution of 1 to 18,000. Browne and Crompton examined 68 cases from 1 to 48 months after the attack. Only 3 gave positive reactions in dilutions of 1 to 20, or 1 to 50. One of these was a case of biliary calculi, and they think that the late reaction was due to the persistence of the bacillus in the gallbladder.

Fison,⁵³ in 21 cases, found 18 that gave a positive reaction from 3 months to 8 years later. Dilutions used were 1 to 2, 1 to 9, in 30 minutes. Renard,⁵⁴ in 104 cases of enteric fever, obtained a positive reaction in 35, 5 of these being 20 years after the attack. Dilutions were 1 to 10.

Stern and S. Klower,⁵⁵ in 100 persons ill with diseases other than typhoid fever, obtained a positive Widal

reaction with the typhoid bacillus in 25 cases, with a dilution of 1 to 10; in 10 with a dilution of 1 to 20; 2 in which a dilution of 1 to 30 was used, and 1 in which a positive reaction occurred in dilution of 1 to 40.

Lagriffoul⁵⁴ in cases of divers affections, including bronchiectasis, brown induration of the lung, syphilis, osteosarcoma of the knee, neurasthenia, disseminated sclerosis, pneumonia of the aged, and 1 case of typhoid fever, found the Widal reaction negative. The reaction was positive, however, in 9 cases of typhoid, 1 case each of articular rheumatism, enteritis, syphilitic fever, and hemichorea.

Zupnik⁵⁷ obtained a positive Widal reaction in 4 of 6 cases of Weil's disease, 6 of cholelithiasis, 1 of cholangitis, 1 of carcinoma of the liver, all of which were complicated by icterus. Eckardt⁵⁸ records 2 cases of Weil's disease in which the blood gave the Widal reaction with the typhoid bacillus in dilutions of 1 to 1,000 after 2 hours. Joachim,⁵⁹ in a patient suffering from purulent cholangitis and one of carcinoma of the ductus choledochus, obtained a positive agglutination reaction with *Bacillus typhosus*, the cholera spirillum and *Bacillus pyocyaneus*. In the latter case the test failed in high dilution, while it was positive in the first case in dilution of 1 to 50. Koehler,⁶⁰ in 10 cases of disease of the liver, of which 8 were icteric, found an agglutination with the typhoid bacillus present in 6. The highest dilution employed was 1 to 50, although 1 to 40 was generally used, and once 1 to 10.

Magale⁶¹ reports an abscess of the liver with positive Widal reaction in dilution of 1 to 100. At the autopsy the findings excluded typhoid. The positive Widal reaction was attributed to the bile in the blood. Libman⁶² claims that the presence of jaundice, leading to a positive Widal reaction, is far from being convincing, as no effort has been made by bacteriologic examinations to determine whether or not typhoid bacilli were present in the gallbladder, feces or urine. Even with dilutions of 1 to 1 he had not obtained any characteristic reaction. In only 4 cases had he obtained a positive Widal reaction in the presence of jaundice.

Koenigstein,⁶³ using mixed cultures of *Bacillus typhosus*, colon bacillus and cholera spirillum with gall (taken from cadavers under sterile precautions) in dilutions of 1 to 10, to 1 to 100, found that in 21 tests there was no positive agglutination reaction; in 2 a partial reaction occurred. He injected 2 dogs with small

amounts of a hemolytic poison which resulted in the production of icterus. The serum before the jaundice developed gave a negative reaction in one dog, while in the second animal a positive reaction occurred in dilution of 1 to 10. The results remained the same after the development of jaundice. Tests made with the serum from patients affected with icterus gave negative results in 7 cases, using the typhoid bacillus. In 1 case agglutination of the colon bacillus was obtained.

Cantani⁶⁴ reports experiments to determine the agglutinating power of bile from normal animals and from those immunized against different bacteria. Bile from normal dogs, guineapigs, oxen and rabbits did not agglutinate *Bacillus coli communis*, *Bacillus typhosus*, *Bacillus influenzae*, staphylococci and streptococci. The bile from animals inoculated with these organisms failed to cause agglutination during the stage of acute infection. On the other hand, when bile from animals highly immunized against a specific organism was used, agglutination occurred rapidly and in high dilutions. The agglutinating power of the bile never exceeded or even reached that of the serum. From these observations the author concludes that if agglutinins are present in the serum in small amount they do not appear in the bile, and when in great quantity in the blood, they may then pass over into the bile.

Pneumococcus.—Rosenow⁶⁵ obtained agglutination with the pneumococcus in 77 out of 83 cases of pneumonia (croupous). Ludwig Jehle,⁶⁶ in 6 cases of pneumonia, came to the conclusion that in all the cases that end by crisis there was present a relatively high degree of agglutinating power in the serum. The power of the agglutination appears at the beginning of the disease and remains to the onset of the crisis. After crisis there is a rapid diminution in the agglutinating power, so that in 48 hours it is present only to a slight degree and in 4 days has entirely disappeared. He suggests that the test may be of diagnostic value in the early stages of pneumonia in doubtful cases. Huber⁶⁷ studied the agglutination of the pneumococcus with the serum of patients having pneumonia. The reaction could be obtained about the fifth day and remained until the crisis.

Tuberculosis.—Arloing and Courmont, in 191 clinically tuberculous patients, obtained a positive agglutination in 87.9%, 12.1% did not give the reaction. Of 130 clinically nontuberculous, 34.6% reacted, 85.4% did not.

Of 41 healthy individuals 26.8% reacted, 73.2% did not. Loeb personally examined 52 cases in which the technic of Arloing and Courmont was followed. His results are as follows: 1. Cases in which blood-serums were used: (a) Nontuberculous, 2+ (100%), 0—. 2. Cases in which serous effusions were employed: (a) Nontuberculous, 6+ (30%), 14— (70%); (b) tuberculous, 12+ (72%), 4— (27%). In 15 cases of pulmonary tuberculosis most of them with bacilli in the sputum, 13 reacted and 2 did not (Lagriffoul). Four of the former were quite cachectic, of these 2 gave the reaction while in the other 2 the reaction was negative. In 5 cases of surgical tuberculosis, all reacted. In 10 cases of pleural effusion all were positive with blood-serum. In 5 cases the serum of the effusion was used and 4 reacted positively and 1 negatively. In 1 case the serous fluid was negative and the blood-serum positive.

Lagriffoul and Pages⁶⁶ claim that the serum of a newborn child of a tuberculous mother does not generally agglutinate the tubercle bacillus. If the agglutinative substance exists in abundance in the blood of the mother a certain quantity may enter the fetal organism.

Marchetti and Stefanelli⁶⁷ conclude from researches in tuberculosis that the serum reaction, applied according to the method of Arloing and Courmont, is positive within the first 6 hours in 43% of cases. In incipient or light cases it gives positive results in 88%. In cases of lupus the reaction was negative, as it was in 9 cases out of 10 in which no clinical symptoms of tuberculosis were present. It should be relied upon as a test only when the reaction occurs during the first 6 hours, as in cases other than tuberculosis the reaction may take place after this time.

Dysentery.—Wollstein⁷⁰ found the Shiga bacillus in 39 out of 114 cases of summer diarrhea of infants. The organisms reacted in 21 cases to the Flexner (Manila) serum in dilutions of from 1 to 50, and 1 to 3,000; while Shiga serum gave the agglutination test in dilutions up to 1 to 200. The serum reaction is uncertain during the first week, frequently positive after the sixth day, but may be absent for 2 weeks. It cannot be relied upon for early diagnostic purposes in infants and young children.

Rosenthal,⁷¹ in 30 cases of dysentery occurring in Moscow, found the reaction absent during the first week, strong from the tenth to twelfth days, and less intense after the fourth week. Fifty-two days was the

latest time in which he was able to obtain an agglutination.

Strong⁷² isolated a bacillus from patients with dysentery in Manila and tested the serum of 100 individuals, some of whom were suffering from various disorders. In 2 a previous history of dysentery was obtained, and 12 were healthy. In all these cases a dilution of 1 to 10 was employed and a time limit of 30 minutes given. A positive reaction occurred in a surgical case and a partial reaction in a specimen of normal blood. Leonard Rogers⁷³ found in cases of dysentery that the serum reaction was present from the sixth day on, but least marked under 10 days.

Duval and Bassett⁷⁴ in 43 typical cases of summer diarrhea in infants succeeded in isolating *Bacillus dysenteriae* (Shiga). The organisms were agglutinated by the blood-serum of patients from whom they were secured, the serum of other infants suffering with summer diarrhea, the serum of patients with acute dysentery, and with antidyenteric immune serum, but not with the blood-serum of healthy children.

Park and Dunham⁷⁵ examined 22 cases of dysentery occurring in different localities and obtained a positive agglutination reaction in 12 cases in dilutions of 1 to 50.

Doerr⁷⁶ in an epidemic of dysentery occurring in an Austrian town (Bruck), observed 168 cases. The bacillus isolated by him was agglutinated always by the serum of convalescents from the disease in dilutions of 1 to 50; some dilutions were used 1 to 200. The serums of individuals from whom the bacilli were isolated did not seem to agglutinate the bacilli any more or less than heterologous serums.

Lawrence B. Pilsbury⁷⁷ in an article upon the agglutination of dysentery bacilli by the blood of noninfected persons, examined 114 cases of diseases other than dysentery. He obtained a positive agglutinating reaction varying from "complete" to "slight" with the bacillus of Shiga in 108 cases in dilutions of 1 to 10; in 93 cases in dilutions of 1 to 20; in 71 cases in dilutions of 1 to 50; and in 29 cases in dilutions of 1 to 100. With Flexner's bacillus agglutination occurred in 93 cases in dilutions of 1 to 10; in 72 cases 1 to 20 dilution, in 33 cases dilution 1 to 50, and in 15 cases with dilutions of 1 to 100. The term "complete" was applied only to those reactions in which no free bacilli were seen and the clumps were large; "good" was applied to those reactions where small clumps occurred and a few free bacilli. This

reaction was especially seen in dilutions of 1 to 20. "Fair" agglutination was applied to those showing fairly good clumps, and when a great many free bacilli retained their Brownian movement to a considerable degree. A "slight" reaction implied one which showed any uniform grouping, however little, well scattered over the field. His conclusions are as follow: 1. That the serum of nondysenteric adult patients does agglutinate the Shiga and acid type (Flexner) bacilli frequently in a dilution of 1 to 20 and occasionally in a dilution as high as 1 to 100. 2. That this agglutinating power is wanting in the blood of nondysenteric young infants (under one year), rarely being present even in a 1 to 10 dilution. 3. That there are certain differences in agglutinating capability between the Shiga and acid type (Flexner) bacilli, the former in these tests, clumping more readily than the latter. 4. That a decided and prompt reaction, under two hours, with *Bacillus dysenteriae* in dilutions of 1 to 20 or higher in young subjects (under 1 year) and 1 to 50 or higher in older persons who have not recently suffered from chronic or subacute intestinal disease, is probably pathognomonic of acute epidemic dysentery.

Flexner¹⁸ claims that the serum reactions of cases of dysentery are of the greatest importance, indicating a close relationship between the bacilli from Japan, Manila, Porto Rico and Germany and rendering probable the identity of the epidemic dysentery of this country with that of the East and Germany. S. Ito¹⁹ has isolated a bacillus from a peculiar form of dysentery in Japan, which organism resembles the colon bacillus. The organism was agglutinated by the serum of patients recovering from the disease, while the serum of normal individuals or of those who had suffered with dysentery or acute enterocolitis had no effect. The serum of patients recovering from the disease did not cause clumping of the dysentery, colon or typhoid group of organisms.

Jürgens,²⁰ in a garrison epidemic of dysentery, comprising 26 cases, isolated from the feces a bacillus resembling that described by Kruse. It differed, however, from the latter organism in its forming acid on mannite agar, and resembled more closely Flexner's bacillus. It was agglutinated by the serum of the patients in dilution of 1 to 100 up to 1 to 500, and even higher, while no agglutination occurred with the bacillus of Kruse.

Hewlett⁸¹ tested a number of cases of dysentery for the agglutination reaction upon a strain of *Bacillus dysenteriae* obtained from Dr. Flexner. All the cases, with one exception, failed to give the reaction, while 2 or 3 cases of other diseases gave the reaction. The case of dysentery which reacted was one of amebic type, though there may have been a double infection. Two fresh cultures of *B. dysenteriae*, a Shiga, and a "Flexner" strain, were used, and of 4 cases of dysentery 3 reacted markedly and the fourth slightly. An amebic case did not react at all. Two cases of asylum dysentery also reacted well. It was noteworthy that these cases reacted with the Flexner strain only and not with the Shiga bacillus.

Hiss and Russell⁸² isolated from a case of enterocolitis in a child an organism that presented many points in common with Shiga's bacillus, but was agglutinated by normal horse serum and antityphoid serum. J. H. M. Knox,⁸³ in a series of cases of infantile diarrhea, from which a bacillus was isolated resembling *B. dysenteriae* (Shiga), obtained a positive agglutination reaction in 10 out of 13 cases during the first week of the disease. "As the reaction persists in the chronic cases for weeks or months, it is in this class of cases that the blood tests may prove useful." Cordes⁸⁴ examined the stools of 51 patients suffering from gastrointestinal diseases. *B. dysenteriae* was found in 26 cases. In 25 the acid mannite type of the bacillus was found; in 1, the alkaline mannite form. Agglutination as high as 1 to 3,000, and 1 to 3,500 was obtained with the bacillus of the acid type in 6 cases. The blood of 45 patients was tested with the Harris and Shiga dysentery bacilli in dilutions of 1 to 40, or 1 to 50, with a positive agglutination in 10 cases.

Bergey,⁸⁵ in an article on the reaction of certain water bacteria with dysentery immune serum, concludes that: 1. The agglutination reaction with dysentery immune serum cannot be relied upon in the differentiation of organisms of *Bacillus dysenteriae* group unless we know the limits of the agglutinating power of the serum employed for the particular organism against which the animal has been immunized. 2. The normal serum of the horse, rabbit, and dog contains agglutinins in relatively small amounts for a variety of organisms. 3. The immunization of an animal against a particular organism increases not only the agglutinins for that organism, but likewise induces an augmentation of the agglutinins of other organisms which are closely related in their

receptor apparatus. Van de Velde⁸⁶ was the first to demonstrate agglutination of streptococci by immune serums. He studied the action of the serum of horses, which were artificially immunized against streptococci (quoted by Weaver⁸⁷). Bordet⁸⁸ observed agglutination reaction occurring between antistreptococcic serum and cultures of *Streptococcus pyogenes*. Salge⁸⁹ found that streptococci isolated from cases of scarlatina were agglutinated by the serum of patients in dilutions up as high as 1 to 500. (Quoted by Weaver.) Wlassjewski⁹⁰ obtained agglutination with streptococci obtained from different sources and an antistreptococcic serum. Serum from a case of puerperal fever agglutinated *Streptococcus pyogenes* in dilutions of 1 to 400.

Moser and Pirquet⁹¹ claim that for streptococci the macroscopic test is more readily done, but the reaction is better observed and the details more evident in the microscopic method. Neither shows an advantage in the constancy of the reaction, both evincing great variations. They injected a horse since the first of the year 1900 with streptococci derived from the heart blood of scarlet fever patients. This serum agglutinated the strain of streptococci injected, microscopically and macroscopically, in dilutions of 1 to 1,000. With one exception, it agglutinated streptococci taken directly from the heart's blood and lymphatic abscesses. The streptococci derived from other sources beside scarlet fever did not agglutinate at 1 to 1,000, but a streptococcus isolated from an empyema gave the reaction in a dilution of 1 to 250. They conclude that streptococci from the blood of scarlet fever patients when cultivated upon artificial media for some time, will agglutinate in an immune serum produced by similar streptococci. They find that agglutination of the streptococcus with the serum of scarlet fever patients occurs in 54% of cases. The agglutination in scarlatina is more marked in severe than in mild cases.

Perkins and Pay⁹² found that some cultures of *Streptococcus pyogenes* isolated from the blood and lesions of variolous patients gave a positive agglutination with the antiserum used in the treatment of variola. The method of Meyer was adopted, in which only those cultures which diffusely clouded bouillon were used. Of 9 cultures tested against the antiserum, only one—and that the one used in the preparation of the serum—was agglutinated by it, while in 2 other cultures there was a feeble reaction, but not conclusive.

H. De Waele and E. Sugg⁸³ isolated a streptococcus from the heart's blood in cadavers dead of variola. This organism was agglutinated by the blood of all patients having variola, and conversely the serum agglutinated any of the streptococci isolated from other cases of small-pox, but not other streptococci, except those which were specific for diseases which the patient passed through. The serum of every vaccinated individual also agglutinated this streptococcus, but less so than after an attack of the disease. The serum of nonvaccinated individuals or of newly-born infants possessed no agglutinating power.

Piassetzka⁸⁴ finds that the antistreptococcic serum of rabbits agglutinates completely homologous streptococci, but that heterologous serum rarely produces a complete reaction, and more often no reaction at all. H. Schiller⁸⁵ points out by experiments that serums which have been produced with virulent and unchanged streptococci agglutinate very promptly all the forms of streptococci. Aronson⁸⁶ has produced a highly valent serum which has brought about agglutination with all forms of streptococci derived from pathologic processes, such as angina, erysipelas, sepsis, scarlet fever, and acute articular rheumatism. As a result of numerous experiments, Weaver has found that of streptococci cultivated from cases of scarlatina, some are agglutinated by almost all scarlatinal serums, but at dilutions varying from 1 to 60, to 1 to 400, others are agglutinated by the same serums with less constancy and at lower dilutions, and many are not agglutinated at all. Streptococci cultivated from cases of scarlatina are agglutinated by serum from cases of lobar pneumonia and erysipelas, in about the same dilutions as by scarlatinal serums, and in the case of erysipelas at even higher dilutions. The same appears to be true of typhoid serum, so far as limited tests indicate, and to almost the same extent of puerperal fever serum. The agglutination reaction between the streptococci cultivated from cases of scarlatina and the serum from cases of scarlet fever is in no way specific, and cannot be of any value as a means of diagnosis. The effects produced by heat and the slight alteration of reaction of the media serve to emphasize the importance of very exact methods in the study of agglutination phenomena in connection with streptococci, as well as with bacteria in general.

Plague.—Wyssokowitz and Zabolotomsky⁸⁷ state that the agglutinative power of the serum in cases of plague is not manifest during the earliest and most acute stage

of the disease. It first appears in the blood about the seventh day of illness, gradually increases until the fourth week, and declines after this period. In cases fatal during the first week of illness they found it absent. Polverini,⁹⁸ in regard to the agglutination reaction in plague, claims that it may not be present in severe cases during the first 10 days of the disease and hence concludes that it is of little value.

In 25 cases of plague Cairns has obtained a positive agglutination reaction in 20 in dilutions of 1 to 10 and 1 to 25. In no case has an undoubted reaction occurred in dilution higher than 1 to 75; quite a number (10) gave the reaction in dilutions of 1 to 50. The agglutinative phenomenon is most marked after the second week of illness, and the agglutinative power, insignificant at the commencement of the illness, progressively increases up to the sixth or seventh week of the disease. It then declines, but may be present in wellmarked cases 4 or 5 months after the primary illness.

Raw⁹⁹ states that the plague commissioners came to the conclusion that the serum diagnosis of plague was of no practical value, inasmuch as while the observation takes at least 20 hours to give pronounced opinion, the clinical features of the disease develop with such rapidity as to leave no doubt of the nature of the disease.

Paratyphoid.—W. P. Johnston¹⁰⁰ reports 4 cases of paratyphoid fever. The serum from 2 of these cases agglutinated the paratyphoid bacillus isolated from the blood. In the other 2 cases the diagnosis was made upon the ability of the patient's serum to agglutinate Gwyn's paracolon bacillus, and the organisms isolated from the other 2 cases. In all 4 cases the Widal test was negative. This report includes Gwyn's case. Of 194 cases of enteric fever in which the agglutination tests were made with the bacillus "O" and Gwyn's paracolon bacillus, the results, except in the 4 cases mentioned, were negative.

Hewlett mentions Achard and Bensaude's¹⁰¹ 2 cases of paratyphoid fever in which the Widal reaction was negative throughout. Agglutination reaction was positive, however, with the bacilli isolated, in 1 case from the urine, and in the other from pus in the right sternoclavicular articulation. He then reports a case coming under his observation in which the serum of the patient gave a positive reaction (with a bacillus obtained from the blood) in dilution of 1 to 100.

Longcope (quoted by Hewlett) reports a case of para-

colon infection in which the serum of the patient gave a reaction in dilution of 1 to 200; with Gwyn's bacillus, at 1 to 500; with the Cushing bacillus, 1 to 200; and "Carlez" bacillus 1 to 20. The serum also agglutinated the typhoid bacillus in low dilution. The work of Cushing,¹⁰² with the bacillus "O," isolated from a costochondral abscess which was agglutinated by the patient's serum in a dilution of 1 to 800, and that of Schottmüller¹⁰³ with cases similar to those of Gwyn is too well known to require elaboration here. Wells and Scott¹⁰⁴ isolated a bacillus which was agglutinated by the patient's serum in dilutions of from 1 to 40, to 1 to 50,000 in cases of paratyphoid fever. Four Widal reactions were made on different days, and all were negative.

Kurth,¹⁰⁵ in 5 cases of Bremen gastric fever, isolated from the feces of one, and from the urine of another, bacilli which were agglutinated by high dilutions of the serum of 4 of the cases.

Brion and Kayser,¹⁰⁶ Libman,¹⁰⁷ and Hume¹⁰⁸ have each observed cases and isolated organisms that resemble yet differ from the typhoid and colon bacilli, which were agglutinated by the serum of the patients.

DeFeyfer and Kayser¹⁰⁹ report an epidemic of paratyphoid fever. Fourteen cases were observed, and the serum of all the cases agglutinated paratyphoid bacilli of the type "A" and "B" of Schottmüller.

L. F. Jermain¹¹⁰ reports 3 cases of paratyphoid fever, the duration of the illness being 16 days. The Widal reaction was negative in each case, though in 1 a serum reaction was positive with Gwyn's paratyphoid bacillus. Kayser¹¹¹ describes 2 organisms isolated from cases of paratyphoid, 1 belonging to the "paracolon group A," and the other to "group B." He thinks that all cases thought to be typhoid fever should be tested with 3 groups of bacteria—the typhoid bacillus and the 2 groups of paratyphoid organisms. The same writer¹¹² observed 3 patients suffering with paratyphoid fever, the diagnosis being made upon the basis of a specific agglutination in high dilutions (1 to 100 and 1 to 1,000) with Schottmüller's paratyphoid bacillus (type B). Bertrand Smith¹¹³ reports 2 cases of paratyphoid infection with positive agglutination reactions in dilution of 1 to 50 up to 1 to 2,000 with the serum of the individual and with the serum of immunized animals. Walker reports a case of paratyphoid fever in which the Widal reaction was negative.

Colon Bacillus.—LeSage,¹¹⁴ in 40 out of 50 cases of

enteritis occurring in infants, isolated *Bacillus coli communis* which was agglutinated by the blood of all the patients.

Johnson and Goodall¹¹⁵ have experimented to ascertain the effect of the action of blood-serum in the different forms of insanity on cultures from mixed strains of *Bacillus coli communis* in order to determine whether by the agglutinins direct evidence could be adduced as to the influence of the colon bacillus in such cases or the indirect evidence of a similar action on the part of other organisms related to the colon bacillus. In all, 25 cases were employed. Good agglutination occurred in 4 out of 5 cases of acute melancholia; 1 out of 3 cases of general paralysis; 1 out of 2 cases of delusional insanity. Partial agglutination appeared in 6 out of 11 cases of acute mania; 1 out of 2 cases of delusional insanity; 1 of alcoholic insanity. No agglutination occurred in 5 cases of mania, 1 of melancholia, 1 of puerperal insanity, 2 of general paralysis, 1 of recurrent mania. Agglutination, therefore, was present in 60% of all cases, in 28% good, and in 30% partial. With control experiments, which were made each time, only 1 showed a slight partial agglutination.

Bruce¹¹⁶ found in the blood in a case of acute mania a short bacillus growing singly, in pairs and chains, which was partially agglutinated by the blood of 5 other patients suffering from acute mania.

Micrococcus melitensis.—Musser and Sailer¹¹⁷ obtained a positive agglutination reaction with *Micrococcus melitensis* in a case of Malta fever. Wright and Smith¹¹⁸ also obtained the same reaction. P. W. B. Smith¹¹⁹ reports a case of Malta fever in an officer, who, after 3 years, still has irregular attacks, and whose blood reacts with well-marked agglutination reaction in dilution of "1 in 40 and over." W. B. Banister,¹²⁰ in a patient who had been in the Philippines where he had been suffering from a fever thought to be malarial, found that the disease presented the clinical features of Malta fever. Serum reaction with *Micrococcus melitensis* was evidenced by marked agglutination.

In Mediterranean fever Aldridge¹²¹ obtained a positive reaction in 30 of 34 cases with *Micrococcus melitensis*.

Miscellaneous.—Vagades¹²² states that we can sometimes show in the blood of patients recovering from influenza a body that gives rise to agglutination of the influenza bacillus.

Wildbölz¹²⁸ observed agglutinating bodies in the serum of guineapigs intraperitoneally inoculated with cultures of the gonococcus grown upon serum bouillon; the animals developed emaciation and other symptoms. He tested old cultures of the gonococcus as well as young cultures and found the agglutination reaction positive. In 2 cases of gonorrhea, one of which presented epididymitis and elevation of temperature, no agglutination reaction occurred, while in the second case the serum reacted with a young culture of the gonococcus and not with an old culture. He also found that the serum of normal guineapigs and the serum of man did not give this reaction with the organism.

Lerch¹²⁴ obtained a positive reaction in 1 case of yellow fever with *Bacillus icteroides* in dilution of 1 to 10 and 1 to 40 upon the second day of illness. Archinard and Woodson¹²⁵ claim to have obtained agglutination with the bacillus of Sanarelli in 75% of cases of yellow fever. Reed and Carroll¹²⁶ have shown that the same reaction occurs with the bacillus of hog cholera in a small percentage of cases of yellow fever. Pothier,¹²⁷ in 154 cases of yellow fever, failed to get a positive agglutination test with *Bacillus typhosus*. In 19 cases the serum reaction was tried with *Bacillus icteroides* with slow clumping and without loss of motility in 8 cases.

J. B. Tombleson¹²⁸ during two successive attacks of yellow fever, found a bacillus in his own blood that he recognized in 6 other cases of the disease. The serum of a dog immunized against the bacillus produced agglutination with young agar cultures. Lowenthal¹²⁹ diagnosed relapsing fever during the apyretic interval when parasites are absent from the blood. The specific agglutination was most marked immediately after the paroxysm, and sometimes became appreciable just before the next chill. When patients overcame the infection, the reaction lasted longer and if it persisted for 7 days in sufficient intensity to cause cessation of motility of the organisms in 1 hour, no further relapses ever occurred. Gabritschewsky¹³⁰ found that the blood of a patient who had just recovered from relapsing fever would cause an agglutination of spirilla in a specimen of blood kept in the thermostat for 30 minutes to 1 hour.

Spronck¹³¹ claims that the serum of lepers, in dilutions of 1 to 60 and 1 to 1,000, agglutinates fresh living cultures of the bacillus of Hansen.

In diphtheria the serum test does not at the present

day figure in the diagnosis of the disease. The bacilli, however, have been agglutinated by antidiphtheric serum by Delepine,¹³² and by Nicholas and Charrin,¹³³ and others. Schwoner¹³⁴ divides the pseudodiphtheria bacilli into 2 groups. The first group, the Hoffman type of organism, is agglutinated partially with normal serum, and completely with monovalent and polyvalent serum, in dilutions of 1 to 10 to 1 to 2,000. In the second group, comprising those bacilli resembling the xerosis bacillus, only homologous varieties are agglutinated with homologous serum.

In tetanus, usually negative results have been obtained; however, Sabrazes and Riviére¹³⁵ by using cultures in a vacuum, obtained clumping with the serum of a patient on the eighth day of the disease. Bordet was the first to show that *B. tetani* was agglutinated by serum of normal horses.

Achard and Lannelongue¹³⁶ have obtained positive agglutination reactions with *Proteus vulgaris* and *Proteus mirabilis* in animals immunized against the organism.

Rogers¹³⁷ found that *Oidium albicans* grew feebly in the serum of animals immunized against it and formed in masses at the bottom of the tube.

Achard and Bensaude obtained a positive agglutination reaction in 10 out of 14 cases of cholera in dilutions of 1 to 10 and 1 to 20.

SUMMARY.

In summarizing it will be seen that of 17,280 cases of enteric fever, 16,352 gave positive reactions and 928 did not; positive, 94.6%.

In paratyphoid fever 42 cases have been collated, and in 40 of these, or 95.2%, a positive reaction was obtained.

In tuberculosis 221 cases were enumerated, and of them 194, or 87.7%, gave a positive reaction.

Of 390 cases of bacillary dysentery 313, or 80.2%, responded to the agglutination test.

In the other diseases only a small number have been reported, hence no reasonable estimate can be given of the percentage of reactions obtainable.

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THE PATHOLOGY OF THE TISSUE CHANGES INDUCED BY THE X-RAY: PRELIMINARY REPORT.

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THE therapeutic efficacy of the X-ray is apparently demonstrated by the results in hundreds of cases of epithelioma, lupus, sycosis, acne, and other lesions thus treated, though time is yet needed to establish the permanency of the cures reported. The clinical effects are much the same in all successful cases—lessening or cessation of pain, drying of discharge if present, smoothing of roughened surfaces, formation of scar tissue. In the case of tumors covered by the skin there is a gradual diminution in size, accompanied or not by softening. The result of overexposure or idiosyncrasy—the so-called X-ray burn—is a well-known, but now, fortunately, very rare complication. Some writers^{1, 2} claim that a reaction, evidenced by a slight dermatitis or its equivalent, is necessary or desirable to obtain therapeutic effects from the X-ray, while others^{3, 4, 5, 6} agree in the belief that this is not essential.

The nature of the tissue changes induced by the X-ray in producing its effects is not clearly understood. Many explanations are offered. Some of these are based on microscopic studies of tissue; others have a clinical foundation, while the only apparent basis of a certain number is the idle speculation of a fertile imagination. With the desire of adding to the knowledge of this question the writer has studied microscopically several tumors, both before and after a series of exposures to the X-ray. This article embodies the results of these

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studies as well as a brief résumé of the theories and findings of other workers gained during a somewhat extensive, though not complete, examination of the more recent literature on the subject.

Oudin, Barthelemy, and Darier,⁷ in a study of X-ray alopecia in guinea-pigs, found the prickle-cell layer and the stratum granulosum ten to fifteen times thicker than the normal, the individual cells being little altered. Not a single hair was visible, and there were only traces of follicles. Hair papillæ, regeneration buds, hair muscles, and sebaceous glands were lacking. The changes in the dermis were trivial compared to those of the epidermis, the connective tissue and elastic tissue networks being normal. The small as well as the large blood-vessels of both cutis and subcutis were normal, and no changes in the nerve fibres were observed. These writers conclude that the X-ray is an irritant of unusual strength, and seems to increase the vitality of the least differentiated skin elements. On the contrary, the differentiated elements—hair, nails, and glands—undergo retrogressive changes and atrophy. They do not know whether these changes are due to nervous influence or to obliteration of vessels or other circulatory disturbances.

Huntington⁸ quotes Rudis-Jicinsky as stating that in the X-ray burn the lesion consists of an acute, subacute, or chronic necrobiosis. In a later article Rudis-Jicinsky⁹ says: "The irritation of the peripheral extremities of the sensory nerves causes a paralysis of the vasomotors of the vascular area affected, spasmodic contraction of the arterioles and capillaries follows, and the proper nutrition of the cells is impaired. . . . With these changes, which are directly dependent upon disturbance of the circulation, there are changes in the parenchyma cells of the affected region. The death of tissue follows, being caused by permanent stasis in the bloodvessels." Huntington also quotes Gassman and Schenkel as finding the intima of arterioles and veins, especially the latter, appreciably thickened and the lumen correspondingly narrowed. This, it is claimed, is due to a deposit of reticular masses of delicate fibrous tissue. Similar processes were noted in the elastica and muscularis.

Lowe¹⁰ mentions Lord Kelvin's demonstration of the fact that an iron bar, electrified and insulated, can be discharged or de-electrified

by the X-ray. He is of the opinion that the dermatitis as well as the therapeutic results may depend upon some similar action on the trophic nerves of the parts exposed.

Veliainoff¹¹ states that Glebovski noted an increase in fibrous tissue, with conspicuous elastica, in cases of lupus and rodent ulcer treated with the X-ray, and also that lymphoid and giant cells underwent fatty degeneration.

Codman¹² coincides with the opinion that attributes these lesions to a primary action on the trophic nerves of the bloodvessels and skin. "The delay in the appearance of the lesions after the exposure, their progressive character, and their failure to react to stimulating treatment are the strongest reasons for this view. The reports of microscopic examination of the excised tissue agree in stating that the smaller arterial branches are occluded, and the appearances are not unlike those of necrosis and inflammation due to other causes."

Pusey¹³ says that carcinomatous masses are replaced by a degenerated, wavy substance without structure and staining a faint blue with hæmatoxylin. The contour of the epithelial cells is lost, and cell nuclei disappear. It is a "degenerative process of some sort, what, cannot be said."

Scholtz¹⁴ says that the X-ray affects, first or entirely, the cell elements which undergo a slow degeneration. This is shown chiefly in the epithelial cells. The phenomena of this degeneration are manifold, the nucleus as well as the protoplasm of the cell being affected. Inflammatory phenomena appear when this degeneration reaches a certain stage. Vessel changes have probably much to do with the further progress and slow healing of ulceration.

Walker¹⁵ has studied sections of a rodent ulcer healing under treatment by the X-ray, and describes the new growth as undergoing fibromyxomatous degeneration.

Blackmar¹⁶ concludes that the X-ray causes a breaking down of malignant and non-malignant growths, the disintegrated material being absorbed. He considers the waste products from a rapidly disintegrating cancer exceedingly dangerous when thrown into the general system unless the patient is in vigorous health.

Morton¹⁷ believes that the effect of the X-ray in the cure of disease

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is due to a primary chemical reaction affecting in turn the metabolic processes. He claims that under proper conditions of administration the X-ray builds up tissue, in proof of which he cites the case of a young woman treated for enlarged axillary glands. In six weeks the neck, shoulders, chest, and breast of that side had developed so markedly that the patient afterward desired the opposite side treated to restore symmetry.

Beck¹⁸ states that an adenocarcinoma subjected to X-ray treatment showed beginning colloid degeneration, changes of the same nature being observed in the epithelium of the skin covering the tumor. Integumental specimens show thickening of the tunica intima of the small bloodvessels, fibrous tissue in reticular arrangement being deposited. The same observer¹⁹ elsewhere states that he places before all the nutritive changes in the walls of bloodvessels and the results incident to such changes.

Bean²⁰ does not think the change is a destructive one. He believes that the cells are restored to their normal condition; and while there may be and often is atrophy connected with the process, there is no necrosis. This statement he contradicts later by saying that in the light of the theory he advances, X-ray burn (really a dermatitis) is what should be expected as the result of too prolonged stimulation, and the necrosis which sometimes follows the dermatitis is the logical outcome of intense inflammation. The theory referred to is based upon the principle of molecular or atomic vibration and its response to heat and light. Bean reasons that the atomic movements of cancer cells and epithelial cells, or of sarcoma cells and connective tissue cells, are not greatly different. If a cell has not wholly departed from its proper atomic motion, we might expect the restoration of that motion or a return to the normal. As the X-rays are probably ethereal vibrations of high frequency, they act by restoring this lost motion to the cell.

Lancashire²¹ says the therapeutic effect is due to mechanical stimulation. The process partakes of the nature of an inflammation.

Loeb²² after seven exposures of ten minutes each during eleven days (transplanted sarcoma in a rat) found mitoses in the cells. The tumor continued to grow, and pieces from it were successfully transplanted into other rats. Degenerative changes were present in the centre of

the tumor, but Loeb states that these changes take place in many tumors without exposure to the X-ray. They were perhaps increased by such exposure.

Herzog²² treated transplanted sarcomas in two rats. The skin over the tumor became necrotic in each case. In one the tumor changed to a cyst filled with a perfectly clear fluid material, and after the fifth exposure the whole tumor came away, leaving a clean surface.

Wiesner²³ claims that the X-ray can act as an irritant to the nervous system, as shown by two cases in which after long exposure of the head to the rays there followed headache, dizziness, vomiting, and diarrhœa. Vomiting and diarrhœa have also followed exposures in the region of the stomach. He concludes that negative ions coming out of the tube penetrate the skin and undergo a chemical change in the molecules or in the nerve endings; this indirectly causes a trophic disturbance. The skin changes are to be looked upon as secondary. This explains the long incubation period of X-ray "burn" and the inaction upon it of therapeutic agents.

Dr. W. M. Sweet, in a personal communication to the writer, assigns to the X-ray a marked effect upon the nerves of exposed areas. In support of this view he mentions the rapid disappearance or lessening of pain in nearly every case treated. In Case II. of this series he removed with a scalpel the projecting portion of the tumor—a mass 2.5 x 3.5 cm. in dimensions—without the aid of anæsthesia and with absolutely no pain to the patient. He also mentions the case of a prominent neurologist who received four four-minute exposures in the effort to locate a supposed foreign body in the eye. Following these the left side of the face became thoroughly anæsthetic to pain and to touch, sensation of heat and cold not being disturbed. The hair also fell out, but later returned. The anæsthesia rapidly diminished.

Hallopeau and Gadaud²⁴ call attention to the sclerogenic action of the X-ray, to which property they attribute the ungual dystrophies and vascular dilatations produced thereby.

Rinehart,²⁵ after stating that he gets no results from X-ray treatment unless inflammatory action is induced, continues: "It then remains to be decided whether the inflammation causes the death of the cancer cells and tuberculous deposits or whether the effect is produced

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by the light itself. My own opinion is that it is the light. Simple inflammation has often been caused by caustics in and around these sores of lupus and epithelioma without producing the death of the process. A light sufficiently strong to produce an inflammation of the healthy cells of the part treated is of sufficient strength to destroy cells of lower vitality, as cancer cells are known to be. Whether the effect upon the skin is produced by the ultra-violet rays remains to be proven. That the low vacuum tube produces more effect upon the skin than the high vacuum tube might help to substantiate the statement that the effect is from the ultra-violet rays, as they are given off more freely from a low vacuum tube."

Freund²⁸ in an article read at the British Medical Association states that in lupus and epithelioma the improvement is due to cell infiltration and proliferation and to the influence of the X-ray in promoting the formation of connective tissue and cicatrices. In his opinion the X-ray possesses no bactericidal qualities.

Bondurant²⁷ states his belief that the effect of the X-ray on cellular metabolism is the essential element in determining its value in the cure of disease, and not its destructive action (of which X-ray burn is an example), nor any supposed germicidal power.

McCaw²⁸ reports the apparent cure of a primary epithelioma of the uvula and soft palate by the use of the X-ray after excision and curettement. After twenty exposures a portion of the remaining growth showed degeneration of the epithelial cells, the protoplasm of which was almost entirely replaced by colloid material. This was not shown in the specimen examined before treatment.

Hett²⁹ believes that destruction of neoplasms does not really occur, because necrosis, if the X-ray is properly applied, does not take place in the cell. On the contrary, the cells seem to have an increased instead of a diminished vitality, this restoring the tissues to their normal condition. This statement seems difficult to reconcile with the following, made a few paragraphs later: "It is a well-known fact that oxygen is set free by the X-ray, and it is probably this factor that produces a change in the neoplasm and embryonic cells by producing disintegration."

Pernet³⁰ examined irradiated lupus vulgaris tissue from beyond the

obviously diseased periphery. The area had been subjected six months previously to fourteen consecutive daily exposures of ten to fifteen minutes each. In some parts the collagen was disjuncted and to some extent disintegrated. The greater part of the elastin had been destroyed. Sweat glands showed surrounding infiltration and signs of disintegration. The hair follicles and sebaceous glands had also apparently disappeared. A large vessel in the subcutaneous stratum showed thickening of its walls. In places there was a fibrous change in the upper layers of the corium.

Leonard³¹ says that the X-ray has both a stimulating and an alterative effect on normal tissues. On tissues of low vitality it has an alterative effect. There may be caused a retrograde metamorphosis, ending in fatty degeneration.

Rieder³² has demonstrated an inhibitory and distinctly bactericidal action of the X-ray on artificial cultures, and the case reported by Shand³³ might suggest this effect on bacteria in tissue. The lesions in Shand's case were recurring superficial abscesses of eighteen months' duration, the pus containing the staphylococcus pyogenes aureus. Improvement began under X-ray treatment, a relapse occurring when treatment was discontinued. Irradiation was again begun and continued until permanent cure resulted.

To this brief summary the writer wishes to add the following observations. For the material upon which the studies were made he is indebted to Dr. J. Chalmers Da Costa and Dr. W. M. Sweet. He also wishes to acknowledge the assistance in the study of tissue and preparation of this report rendered him by Dr. W. M. L. Coplin, who also suggested the idea and method of securing exposures of only a part of the tumor in Case I. This was accomplished by the use of a lead shield in which was made an opening corresponding in size and shape to the part to be exposed. By orienting this opening with the nipple at each application comparatively accurate placing was obtained, the exposed area being outlined with caustic at the time of the last exposure. Before the breast was removed two deep silkworm-gut sutures were passed to anchor the skin firmly to the underlying tissues, and before the removed specimen was incised the skin was further immobilized by inserting a row of sutures in the boundary of the outlined area.

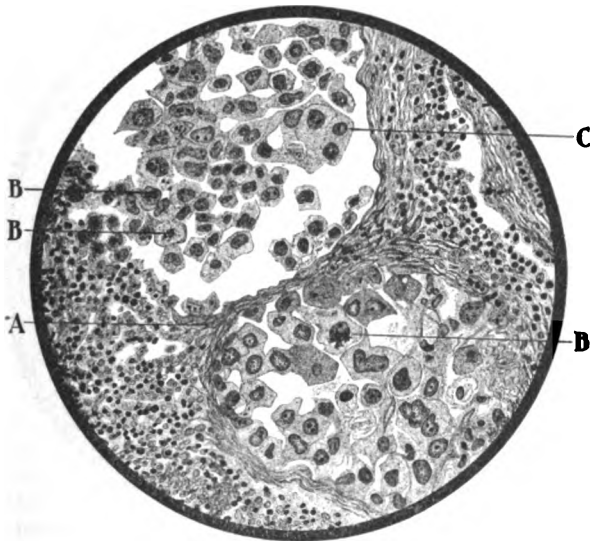
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In the examination of the tissues upon which this report is based the following technique was employed: Tissue, except that for study of the nerves, was fixed in corrosive sublimate solution, hardened, and dehydrated in alcohol, and infiltrated with paraffin. Sections were stained with hæmatoxylin and eosin, hæmatoxylin and picric acid, and hæmatoxylin and Van Gieson; also with toluidin blue, Weigert's elastic tissue stain, Ehrlich's triacid mixture, and by Pianese's stain for differentiating hyalin, mucin, and colloid. Tissue for nerve study was fixed in Müller's fluid, dehydrated in alcohol, and infiltrated with celloidin, sections being stained by Weigert's method for myelin. Other pieces of the nerves were prepared by the method of Marchi.

CASE I.—M. W., aged forty-five years, patient of Dr. Da Costa. A tumor in the left breast was first noticed in July, 1901. This increased in size until February, 1902, when it was the size of a hen's egg. Both the tumor and breast were movable, but there was axillary involvement. This proved so extensive that much of the growth could not be removed at the time of operation. It afterward grew rapidly, œdema and pain became intense, and the patient when last seen was sinking rapidly. The inner half of this tumor was given eight ten-minute exposures to the X-ray at intervals of two to three days. After the fifth treatment the exposed portion of the tumor became noticeably softer. Operation was performed March 29, 1902, by Dr. Da Costa, the specimen received for examination being the entire breast and axillary glands. Palpation showed the exposed area to be distinctly softer than the remainder of the tumor, especially the lower end, where slight fluctuation could be detected. A needle prick into the breast just within the line separating the exposed from the unexposed areas was followed by the escape in jet of a fluid resembling serous pus. Incision of the exposed area showed surfaces studded with small, yellowish areas, apparently fatty in nature. This appearance gradually diminished toward the depth of the mass, except at the lower end, where there existed a partially filled cavity, 0.5 x 1.5 cm. in dimensions. This cavity approached closely to the skin at the point pricked by the needle, and contained fluid resembling that evacuated by the puncture. The tissue surrounding this cavity showed the yellowish, fatty appearance to a marked degree. Microscopic examination of the fluid showed it to contain a moderate number of large cells, 12 to 16 μ in diameter, having hyaline protoplasm and granular nuclei. Treatment with Sudan III. and osmic acid showed these cells to be practically filled with fat granules. In addition the fluid contained red and white (lymphocytes) blood corpuscles and granular debris.

Sections from the unexposed portion of the tumor (Fig. 1) show it to be a scirrhus carcinoma. In many portions of the sections are dense collections of lymphoid cells. A few polymorphonuclear leucocytes and plasma cells are also seen. There are fairly numerous thick-walled bloodvessels, but very few of these show evidence of deposits on their inner surfaces. Staining by Gram's method shows the presence of a large number of small hyaline bodies resembling the so-called corpora amylacea. Mitotic cells are fairly numerous. Plimmer's bodies are present. No bacteria are demonstrable.

FIG. 1.



CASE I.—Scirrhus carcinoma of mamma. Section from unexposed area. A. Scanty stroma separating two alveoli. In the upper right and lower left parts of the field the extensive lymphoid and plasma-cell infiltration of the stroma is well shown. B, B, B. Cells showing atypic mitoses. C. Cells showing fusion of the protoplasm, formation of the so-called giant cells of cancer.

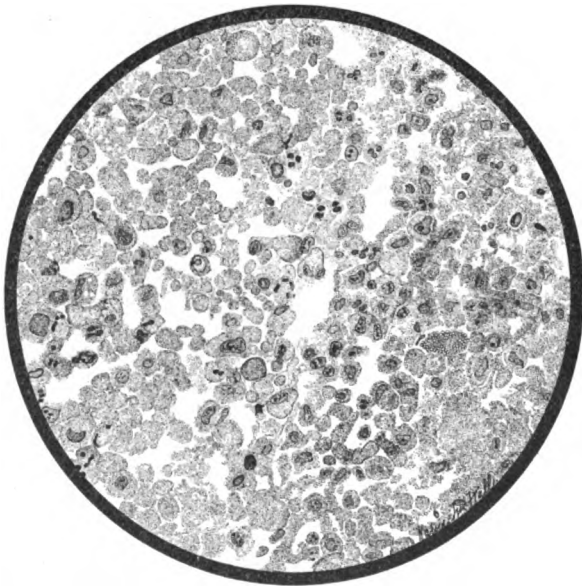
Technique: Tissue fixed in Heidenhain's corrosive sublimate solution, paraffin infiltration, hæmatoxylin, and Van Gieson. B. and L. $\frac{1}{6}$ in. obj., 1 in. oc.

Sections from the exposed portion show the same general characteristics (broadly speaking), but the following differences are noted: 1. There are large areas of necrotic tissue, especially in those portions which border on the cavity described. (Fig. 2.) Some of the necrotic

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material is homogeneous in appearance, while other portions show the outlines of large cells, the protoplasm of which is in various stages of vacuolization and fragmentation, the nuclei having disappeared. Near the junction of these necrotic areas with the less conspicuously altered tumor are detached clusters of epithelial cells, the protoplasm of which has fused, the nuclei being in various stages of degeneration. The cells of the tumor bordering the necrotic area also show the changes

FIG. 2.



CASE I.—Scirrhus carcinoma. Section from exposed area. Field includes the contents of a large alveolus. Plasmatolysis and chromatolysis, which in parts of the section have terminated in the formation of a finely granular acidophilic detritus, are present throughout the field.

Technique: Tissue fixed in Heidenhain's corrosive sublimate solution, paraffin infiltration, hæmatoxylin, and Van Gieson. B. and L. $\frac{1}{6}$ in. obj., 1 in. oc.

just described, the degree of change becoming less as the distance from the necrosed area increases; but degenerative or necrotic changes in some degree are present in practically all the epithelial cells of this portion of the tumor, and distinct areas of beginning necrosis are scattered throughout. Special staining as well as the reactions to ordinary stains

show that this degenerated material is not colloid in nature. 2. Collections of lymphoid cells are very few in number as compared with those in the unexposed portion. In the necrotic areas are a very few cells resembling polymorphonuclear leucocytes, but it is difficult to say whether they are such or are greatly changed epithelial cells with fragmented nuclei. My belief is that they are the latter. 3. Very few of the small hyaline bodies are present. 4. Some bloodvessels show endarteritis, deposits on the inner surface partially or almost wholly occluding them. 5. No mitoses are seen. Plimmer's bodies are not present in the most necrotic areas, but in other portions appear to be as numerous as in the unexposed areas. Elastic tissue is apparently more abundant than in the unexposed sections.

CASE II.—W. N., aged fifty-seven years, patient of Dr. Sweet. Lymphangio-endothelioma of the orbit. The growth involved the nose and frontal sinus, and was making its appearance at the inner canthus of the opposite eye when the patient entered a distant hospital and was lost sight of. This tumor was not examined until after five ten-minute exposures to the X-ray, no tissue having been removed before treatment was begun. Sections of the tumor have for the most part a scanty fibrous tissue stroma inclosing alveoli lined with from one to several layers of large polymorphous endothelial cells. The alveoli contain masses of cells showing varying degrees of necrosis. In a few instances the outline of the cell is distinguishable, as is also the nucleus, the protoplasm being markedly vacuolated. The greater number of the cells do not show a distinct outline, the protoplasm being indistinct or irregular, or has even partially disappeared. The nuclei of these cells are fragmented, the fragments staining deeply with basic dyes. In some cells the process has gone still further, only a homogeneous material with no evidence of nuclei being present. In many of the alveoli the lining cells show the same beginning degeneration. Some of the larger necrotic areas have undoubtedly been formed by the fusion of several alveoli, as in them fragments of degenerating trabeculae are seen, more commonly near the periphery. Bloodvessels are fairly numerous and have very thin walls. No bacteria are demonstrable. Mast cells are present. Elastic tissue is very scanty. The necrotic changes in this tumor, though less advanced, are the counterpart of those found in Case I.

CASE III.—F. M., colored, aged fifty-two years, patient of Dr. Da Costa. Ulcerated area, 9 x 12 cm. in size, of one year's duration, on inner aspect of right knee, having developed in the scar of a burn received when the patient was eight years of age. Examination of a small bit of tissue removed showed it to be a typical squamous-cell epithelioma containing an unusually large number of keratinized areas,

the so-called pearls. Collections of lymphoid cells were numerous. X-ray treatment was begun and twenty ten-minute exposures of about two days' interval given. Improvement was slow, and, excessive pain persisting, the leg was amputated. Examination of the removed tumor shows only a moderate change as a result of treatment. Collections of lymphoid cells are equally numerous. Bloodvessels show an increase of fibrous tissue, with fragmented inner elastic layer. The lumen of some is occluded. Epithelial cells in areas most free from pearls show varying degrees of necrosis, as vacuolization, fusing of protoplasm, and fragmentation of nuclei. These changes can scarcely be detected in areas composed mainly of pearls, which are very numerous. Elastic tissue is very abundant, apparently an increased amount over that found in sections from the tumor before exposure. Sections stained with toluidin blue and by Gram's method show cocci and bacilli of various sizes to be exceedingly numerous. Sections of the internal popliteal nerve underlying the tumor after being treated by Marchi's method show fatty degeneration and fragmentation of some of the myelin sheaths. These changes appear to be partly of recent origin and partly of longer duration. Bloodvessels of the nerve show endarteritis, the lumen of many of them being almost obliterated.

CASE IV.—R. B., aged thirty-two years, patient of Dr. Sweet. Large ulcerated surface on side of head, of ten years' duration. Growth extends posteriorly two inches behind the mastoid process and anteriorly to the orbital ridge, the ear being entirely gone. On August 7th a bit of tissue was removed for examination, which proved the growth to be a squamous epithelioma containing a few pearls. On August 14th treatment was begun. On August 29th a second piece of tissue was removed and examined, ten ten-minute exposures to the X-ray having been given. Though the clinical results were most satisfactory—cessation of profuse discharge, smoothing and healing of granulating surfaces, disappearance of pain—the microscopic changes are the least of any case examined. There is an increase of elastic tissue. In a few areas there is slight evidence of a beginning degeneration in the epithelial cells, but this is nowhere advanced. Infiltration of lymphocytes is about equal in the two specimens. Vessel walls show slight if any change. The report from this case, October 3d, is that healing still continues, but the portion of the growth from which the second specimen was removed shows the least progress. The affected area is so large that not all is exposed to the X-ray at each sitting. This probably accounts for the slight changes observed in the tissue after irradiation.

To summarize, the study of these cases shows: 1. Necrosis of cells and trabeculæ of varying degree. In Case I. there is also marked

fatty degeneration. 2. Increase of elastic tissue in the three cases examined both before and after exposure. 3. Fewer areas of lymphocytic infiltration in one case after exposure, about equal numbers in the others. 4. A tendency to occlusion of vessels by deposits on their inner surfaces. This is marked in some instances, not so prominent in others. 5. Practically entire absence of infiltration by polymorphonuclear leucocytes.

Conclusions are hardly warranted by the results of these examinations, especially as further studies are being made with reference to nerve changes in irradiated tissue. Investigations regarding blood changes in persons undergoing this treatment and the tissue changes in normal rabbits that have been X-rayed are also under way. A few thoughts, however, suggest themselves:

1. Beck and others lay great stress on bloodvessel changes as the cause of necrosis. While endarteritis is probably induced by the X-ray, the accompanying tissue necrosis seems out of proportion to the vessel changes, suggesting the possibility of these being *pari passu* results of the same influence, instead of cause and effect.

2. The presence of immense numbers of cocci and bacilli in the tissues of Case III. after twenty exposures to the X-ray would argue against the possession by that agent of bactericidal power. It should be said that the pathogenicity of these organisms was not proven.

3. The unsatisfactory clinical results as well as the slight microscopic changes in Case III. can probably be safely attributed to the presence of the exceedingly numerous keratinized areas or "pearls." This emphasizes the importance of curetting or cutting away diseased tissue, whenever feasible, before instituting treatment by the X-ray.

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THE BACTERIOLOGY OF OTITIS MEDIA: A SUMMARY OF RECORDED OBSERVATIONS AND A LABORATORY STUDY OF 76 CASES.*

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It may be well to state in the beginning that this article deals only with the bacteriology of diseases of the middle ear, and that the innumerable infections, including bacteria, yeasts, molds, etc., in the auditory canal have been considered only when they possess a direct bearing on the subject under immediate review. While the literature of mycoses of the external auditory canal might have been incorporated in the present work, it has been deemed wise to omit it, as but little of special interest or great practical import has been recorded between the observations of Mayer,¹ who in 1844 observed *Aspergillus* in the external auditory canal, and the more recent work, such as Highet² on Tropical Otomycosis.

BACTERIOLOGY OF THE NORMAL EAR.‡

Preysing³ examined the tympanum in 45 postmortems; of these, 6 cases can be excluded, as gross evidence of disease was clearly present; of the remaining 39 cases, in 32 both ears were sterile, in 3 cases 1 ear was sterile and the other infected, and in 4 cases both ears were infected without gross evidence of any lesion. When the possibilities of accidental contamination are considered, the author's conclusion that the normal ear is sterile seems fully justified by his own research.

Zaufal,⁴ by experiments on rabbits, reached an oppo-

*Professor S. MacCuen Smith offered a prize for the best thesis embodying data included in the above title, and the following is an abstract based upon the thesis submitted.

†From studies made in the laboratories of the Jefferson Medical College Hospital. I wish at this point to acknowledge the supervision and aid given by the director of the laboratories, Prof. W. M. L. Coplin, and his assistants. For the clinical material I am indebted to Professor Smith, Dr. William Welch and his assistant, Dr. Sutton, of the Municipal Hospital; Drs. Klopp and Hoopes, of the Otologic Department of the Jefferson Hospital.

‡Part I, dealing with the Anatomy of the Normal Ear, and, to a certain extent, with its Embryology, is omitted in this abstract.

site conclusion; the largest number of bacteria are found near the eustachian opening in the pharynx, but decrease in number as we approach the tympanum, which may be sterile. In 50% of the cases examined by DeRossi,⁵ streptococci and various bacilli were found during life. This examination embraced only the eustachian tube. Kossel,⁶ in 85 of 108 postmortems on infants under 1 year, found the tympanum diseased, and Rasch⁷ found 5 normal tympanums in 61 postmortems on children under 2 years of age. In Hartmann's⁸ series the tympanum was normal in 10 out of 47.

To the foregoing I desire to add 1 case:

A man, aged 46 years, died of tetanus. The bacillus was found by Dr. R. C. Rosenberger in the ulcer of the leg, but not in the meninges, brain or tympanic cavity. The *Staphylococcus pyogenes albus* was found in the left tympanum, the right was sterile.

The somewhat contradictory opinions based upon observations of other writers can be explained only by the assumption, as their findings indicate, that the conditions which determine the presence or absence of bacteria from the middle ear in health, are not sufficiently well known to justify positive statements on the subject. As pointed out by Zaufal, the condition of the eustachian epithelium probably more than anything else, influences the presence or absence of bacteria in the tube and drum cavity. With normal epithelium, normal drainage, and normal resistance, it seems improbable that bacteria ever reach the middle ear in sufficient numbers to give rise to any disturbance in the normal organ. To this, of course, there must be an occasional exception. The finding of bacteria, postmortem, may be due to agonal dissemination or, as pointed out by Ford,⁹ healthy organs may contain bacteria. With a few exceptions, the pathogenicity of the bacteria found has not been tested, but it is probable, from a study of the literature on the subject that bacteria of a low order of virulence may inhabit the middle ear without producing any phenomena until weakened resistance renders invasion possible.

Does otitis media occur in the absence of bacteria? A number of Preysing's cases indicate such a possibility, and Scheibe's¹⁰ reported cases contain one or two instances in which the bacteria present were not, probably, initially the cause of inflammation. Modern research seems to indicate that inflammation of glandular structures may result from obstruction to the outward flow of secretion as is observed in cholangitis and interstitial

hepatic changes secondary to the obstruction of the biliary channels, interstitial mastitis secondary to obstructive lesions in the galactophorous ducts, and pyelitis resulting from ureteral obstruction, and a number of other conditions that need not be mentioned. Every catarrhal discharge offers a most suitable nidus for the subsequent colonization of pathogenic bacteria or, it may be, enhances the virulence of organisms that, under otherwise normal conditions, would not induce lesions amounting in intensity to what we would term an inflammation. Every tympanum containing retained catarrhal matter is a mine, the explosive character of which becomes evident immediately on the introduction of pathogenic bacteria.

PORTAL OF ENTRY.

While a number of workers have devoted their energies to this aspect of middle ear infections, it is to Moos¹¹ that we are indebted for a careful exposition of the possible routes by which bacteria may reach the tympanic mucosa or enclosed cavity. According to this author the following should be considered: I. *Hematogenous*. II. *Eustachian tube*. III. *By way of the tympanic membrane*. IV. *Through the petrosquamous fissure*.

I. As proof of the possibility of infection from the blood, Moos cites the intrauterine infection of the fetus by bacteria-laden maternal blood. In Levy's case the pleural effusion of the mother and the blood of the right ventricle of the child produced pneumosepsis in animals. Trautmann¹² has recorded what appears to be an infection from verrucose endocarditis. Zaufal admits the possibility of hematogenous infection, and found pneumococci in the tympanic cavity of animals inoculated with the organism. Lermoyez and Helme¹³ believe that hematogenous infection gives rise to a more violent and more acute process than eustachian infection.

II. *Eustachian Infection*.—As already indicated the normal eustachian tube is inhibitory but not prohibitory to bacterial invasion. Zaufal's demonstration that the pharyngeal end of the tube frequently contains bacteria, renders it necessary only to assume that reduced resistance permits extension and thereby infection of the drum cavity. Eustachian instrumentation in preaseptic days was undoubtedly a frequent cause of infection. Zaufal and Moos¹⁴ believed that forced expiration, with the mouth and nose closed, may drive infecting sub-

stances into the tube; Zaufal, Lermoyez and Helme, Moos, and most authors, believe that politzerization possesses the same dangers. Lermoyez and Helme believe that such dangers are less in the presence of an intact drum. They believe that pneumococcal infection occurs from the pharynx and staphylococcal invasion through the tympanic membrane. Profound anemias, tuberculosis and other chronic infections, acute infective processes, such as diphtheria, scarlatina, measles, pneumonia, influenza, smallpox, etc., and even the simpler anginas, and allied processes, may favor the occurrence of infection in two ways: (1) Locally they influence the nutrition of the cells of the eustachian tube, whose activity under normal conditions is directed toward the removal of infected or infective material; (2) they reduce the protective power manifested by the leukocytes, the body juices and the tissues against invasion, and possibly, at the same time, increase the virulence of organisms present. Such processes weaken the garrison and stimulate the attacking enemy. Netter¹⁵ is clearly of the opinion that bacterial ingress occurs from the pharynx. Rohrer¹⁶ in part, coincides with this view. Most authors are agreed that the same organisms are found in otitis as are observed in the pharynx and nasopharynx, and the frequency of the pneumococcus otitis is explained if we recall Weichselbaum's¹⁷ observations concerning its frequency in and around the eustachian orifice in pneumonia.

III. *Infection Through the Tympanic Membrane.*—The majority of the infections reaching the middle ear through the tympanic membrane are secondary to its rupture, but Moos¹¹ has observed extension of erysipelatous inflammation through the unruptured drum. Infections of the middle ear consecutive to perforation of the drum, as by foreign bodies, wounds, primary suppurations in the auditory canal, and infections and ulcerations due to foreign bodies need be mentioned only.

IV. *Infection Through the Petrosquamous Fissure.*—Klebs¹⁸ first demonstrated this route of infection in epidemic cerebrospinal meningitis, and Moos¹¹ in ordinary (!) meningitis. Little is known of this path of infection, and under ordinary conditions, as the fissure closes long before adolescence, it must be inconsequential. The exception must be in those rare cases in which the fissure persists in adult life.

Other Routes of Infection.—As pointed out by Zaufal

there is a rich submucous lymph plexus in the pharynx and nasopharynx, which is continuous with a similar plexus surrounding the eustachian tube. Weichselbaum has demonstrated the serous infiltration and microbic invasion of the pharyngeal part of this lymph system, and by reason of its abundant anastomosis with the perieustachian lymphatics, extension to the middle ear must be regarded as a possibility. Lionel de Crevoisier and de Vomécourt¹⁹ state that localization in the ear results from the imperfect drainage of the canal and the favorable culture soil in the adjacent bone. Hirsch²⁰ in his study of diphtheritic otitis believes that extension occurs by the bloodvessels or lymphatics as in the case examined the change in the tube was inconspicuous compared with the otitic lesions.

With regard to the relative importance of these various paths of entry, the eustachian route probably deserves a preeminent position. Hematogenous infection is infrequent, but grave, by reason of the associated blood mycosis. Lymphogenous infection is probably infrequent, but still an admitted possibility. The petrosquamous fissure may afford a path of entry to the middle ear, or may offer a favorable route for extension to the mastoid. For further discussion of this subject see Moos^{11, 21}, Gruber²², Kirchner²³, Kiesselback²⁴, and Bezold²⁵ who have extended our knowledge of the subject.

BACTERIA FOUND.

Review of Earlier Observations.—Loewenberg²⁶ recognized the presence of globe and staff bacteria in otitis media, and, although skeptical as to the exact role of the organisms found, introduced, in its then crude form, the antiseptic treatment of suppurating ears. Loewenberg believed that bacteria were secondary invaders and not the cause of the otitis. It is quite impossible from his description to say definitely what organisms were observed.

*Pneumococcus.**—Almost coincident with the demonstration of the pathogenicity of this organism, by Pasteur²⁷, Sternberg²⁸, Frankel²⁹, Netter³⁰ and Weichselbaum³¹, its association with otitis was recognized. Zaufel³² credits Netter with having been the first to demonstrate its presence in the fluid contents of the labyrinth in a case of pneumonia complicated by meningitis;

* While most difficult to follow a definite order an attempt will be made to take up first cocci, later bacilli and other organisms found.

later he found the organism in the secretion of the nose and sphenoid sinus. In a series of papers the bacteriology of otitis media, the paths of infection, the associated conditions and complications, and the bacteriology of the disease, have been elaborately considered by Zaufal^{33, 34, 35, 36, 37}. He also noted the fact that otitis may clinically resemble pneumonia in the occurrence of chill, a critical period, a fall of temperature, and absorption of the exudate. Clinical records show that otitis is prevalent synchronously with pneumonia; 1,205 cases of otitis and 1,165 of pneumonia. Pneumonia may be secondary to otitis or otitis may occur as a complication to pneumonia. As pneumonia may go from one lung to the other so otitis may go from one ear to the other. Zaufal produced otitis media in rabbits and guineapigs by the inoculation of the tympanum, and considered the possibility of otitic inflammation secondary to meningitis as well as the reverse. He demonstrated the pneumococcus in a mastoid abscess complicating otitis media, and observes that of 15 cases of pneumococcal otitis 5 were complicated by mastoid abscess. Senger³⁸ found an organism which he believed to be the pneumococcus in 4 cases of suppurative meningitis, secondary to otitis media. Leyden³⁹ records a similar observation. Weichselbaum⁴⁰ found the pneumococcus in the tympanum in 4 out of 5 cases of cerebrospinal meningitis. Frankel⁴¹ concluded that the pneumococcus preserves its vitality and virulence longer in fluids, a view that is fully in accord with the established recrudescence of pneumococcal otitis and late mastoid disease due to the pneumococcus. Netter¹⁵ came to the conclusion that otitis media may be due to a number of microorganisms, and recognized 4 distinct forms of the acute type: (1) Streptococcal, (2) Pneumococcal, (3) Pneumobacillary (Friedländer), (4) Staphylococcal. The pneumococcal according to this writer is less grave than the streptococcal. In Röhrer's investigation of 100 cases of otitis media there can be no doubt from his description that many were due to the pneumococcus. Lermoyez and Helme,¹¹ Lionel de Crevoisier and de Vomécourt,¹⁹ Gradenigo,⁴² Levy and Schrader,⁴³ Levy,⁴⁴ Weichselbaum,⁴⁵ Finkler,⁴⁶ Kanthack,⁴⁷ Scheibe,^{10, 48} Bordoni-Uffreduzzi and Gradenigo,⁴⁹ Müller,⁵⁰ Gradenigo,⁵¹ Maggiori and Gradenigo,⁵² Gradenigo, Bordoni and Penzo,⁵³ Talamon,⁵⁴ Rist,⁵⁵ Chambers,⁵⁶ Hirst,⁵⁷ and Heinemann,⁵⁸ have recognized the pneumococcus as a cause of otitis media and from their writings and other authors already quoted in this paper,

the following table showing the frequency of pure pneumococcal infections, as well as mixed infection, has been compiled :

Pneumococcus in pure culture.....	151
" " with Streptococcus	22
" " Staphylococcus.....	26
" " Streptococcus and Staphylococcus.....	1
" " Bacillus saprogenes.....	3
" " Bacillus pyocyaneus.....	2
" " Bacilli pyocyaneus and saprogenes.....	1
" " Staphylococcus and Bacillus saprogenes	3
" " Bacillus coli communis.....	3
" " Micrococcus tetragenus.....	3
" " Streptococcus, Staphylococcus and Bacillus saprogenes.....	1
" " Pseudoinfluenza bacillus.....	10
" " Bacillus subtilis.....	2
" " Nonpathogenic bacilli.....	1
" " Nonpathogenic bacilli and Staphylococci.....	2
" " small bacilli (unidentified)	2
Total.....	232

Streptococcus.—Netter⁵⁹ found the streptococcus in the meningeal exudate in a case of meningitis with caries of the petrosal portion of the temporal bone, and Moos⁶⁰ observed it in the labyrinth in a patient dead of diphtheria, and in another dead of measles. Zaufal found the streptococcus in a number of his cases, and considers the organism a most important agent in the production of acute otitis; he claims that such infection is extremely prone to be complicated by mastoiditis, labyrinthitis, meningitis, encephalitis, sinus thrombosis and pyemia. Streptococcal infections are graver than pneumococcal and staphylococcal infections. Streptococcal infections are frequently single, but the organism shows a decided tendency toward grouping with other bacteria, and probably more than any other microbe, exists as mixed infection. It frequently occurs with the pneumococcus, and primary pneumococcal otitis may become streptococcal. It is a common cause of the meningitis associated with acute infections such as measles, scarlet fever, typhoid, etc. According to the investigations of Seitz,⁶¹ Dunin,⁶² Frankel-Simmonds,⁶³ Hengst,⁶⁴ Destree,⁶⁵ Vincent,⁶⁶ Prochaska,⁶⁷ and others, the usual etiologic factors in the otitic suppurations of typhoid fever are the pyogenic organisms, and of these the streptococcus plays an important, if not predominant rôle. Moos attributes to the streptococcus and pneumococcus the most important position in the production of an acute otitis; he has found them in chronic cases, although Kanthack and Gradenigo have not.

Dunin,⁶⁶ Holst,⁶⁶ Bezold,⁷⁰ Scheibe, Moos, Zaufal, and a number of others have written upon streptococcus infection of the ear with numerous reported cases. According to Hubner⁷¹ and Blaxall⁷² the streptococcus is the most common organism in scarlatinal and diphtheritic otitis. Guinon⁷³ admits otitis as a complication of erysipelas, a view corroborated by Moos; Lippincott⁷⁴ reported cases of otitis following erysipelas. Würdemann⁷⁵ reports 3 cases of erysipelas complicated by otitis media, and Hessler⁷⁶ reports the occurrence of erysipelas secondary to otitis media. The correlation of erysipelas and otitis has been noted by Cornil,⁷⁷ and Mackenzie and Schwartz.⁷⁸ Moos has noted its association with the tubercle-bacillus; the same writer⁷⁹ has observed its connection with pyemia and septicemia due to otitic complications. Raskin⁸⁰ and Moos support Blaxall's contention that the pneumococcus is infrequent in scarlatinal otitis, and the streptococcus is usually present. Thomas⁸¹ reports a fatal case in which the streptococci predominated, and in which staphylococci were also present; his case may be taken as a fair type of the widespread lesions that may be caused by this organism; there were scarlet fever, tonsillitis, submaxillary and cervical swelling, otitis media, general pharyngitis with retropharyngeal abscess, acute purulent inflammation of the nares and nasopharynx, and pseudomembranous enteritis. J. Aschkinose⁸² also notes the occurrence of streptococcus otitis.

Sufficient data are not available to establish exactly what organism predominates in cerebral abscesses. According to Jansen (quoted by Schubert⁸³) it occurs once in 2,650 cases of acute otitis and 5 times in 2,500 cases of chronic otitis. As the pneumococcus is frequent in the former, and the staphylococcus and streptococcus in the latter, it would be reasonable to assume that the latter organisms play a predominant role in the production of suppurative cerebritis. That the streptococcus may be found alone is proven by the case reported by May.⁸⁴

TABLE.

Streptococcus in pure culture.....	80
" with Pneumococcus.....	22
" " Staphylococcus.....	21
" " Staphylococcus and pneumococcus.....	1
" " Staphylococcus and Bacillus diphtheriae.....	8
" " Staphylococcus, pneumococcus and Bacillus saprogenes I.....	1
" " Staphylococcus and Bacillus pyocyaneus.....	2
" " Staphylococcus and nonpathogenic bacilli.....	3

Streptococcus with	Bacillus pyocyaneus.....	2
"	Staphylococcus, Bacillus striatus albus, Micrococcus liquefaciens albus, Bacil- lus subtilis and Sarcina lutea and alba.....	1
"	Bacillus pyocyaneus and spirilli.....	1
"	Staphylococcus and Bacillus striatus albus.....	2
"	staphylococcus, Bacillus striatus albus and forula.....	1
"	Bacillus acidilactici, saprophytes, Staphylococcus, yellow yeast and un- known bacteria.....	1
"	Bacillus striatus albus and Aspergillus niger.....	1
"	Staphylococcus, Bacillus tuberculosis, Aspergillus niger and Penicillium glau- cum.....	1
"	Bacillus striatus albus, white yeast and an unidentified Diplococcus.....	1
"	Bacillus striatus albus, pink yeast and Sarcina lutea.....	1
"	Bacillus tuberculosis.....	5
"	Bacillus pseudoinfluenzae.....	4
"	Bacillus pyogenes foetidus.....	4
"	Staphylococcus, Staphylococcus parvu- lus and Bacillus perfringens.....	1
"	Staphylococcus foetidus, Micrococcus foetidus, an unnamed coccus and an unnamed bacillus.....	1
"	Bacillus coli communis.....	1
"	Streptococcus tenuis of Veillon, Bacillus ramosus and an unnamed bacillus.....	1
"	Staphylococcus, Bacillus striatus albus and Oidium albicans.....	1
"	Staphylococcus, Bacillus striatus albus and Micrococcus liquefaciens albus.....	1
"	Staphylococcus, Bacillus striatus albus, Micrococcus liquefaciens albus and pink yeast.....	1
"	Staphylococcus and Bacillus pyogenes foetidus.....	3
"	unidentified bacteria.....	3
Total.....		178

Staphylococci.—Previous to the reports of Haberman⁸⁵ but few instances of staphylococcus infections of the middle ear had been recorded. Maggiori and Gradenigo⁸⁶ observed *S. aureus* 7 times, *S. albus* 8 and *S. cereus albus* twice in 20 cases. In a number of these cases the organisms were associated, and in nearly all saprophytic organisms were present. Burnett⁸⁷ reports a staphylococcal otitis which he believed was due to the use of a nasal douche. Bulling,⁸⁸ Kirchner,⁸⁹ Stern,⁹⁰ Merritt,⁹¹ Pollak⁹² (?) and many of the writers already quoted report the finding of staphylococci in otitis media. Staphylococcal infections are usually chronic, and it is commonly held that the staphylococcus is implanted upon a previous pneumococcal or other infection. In the cases collected by Martha⁹³ 25% contained staphylococci when examined within 3 months after the initial

inflammation, and 64% in later examinations. Kossell,⁹⁴ Chatterlier,⁹⁵ Legendre and Beausseate⁹⁶ and Kanthack⁹⁷ have shown that staphylococci may be present at the initial paracentesis. Lermoyez and Helme observe that staphylococci are rarely present in acute suppurative process, but occur with increasing frequency as the process grows old, and that they are found in 92% of the old otorrheas. According to these authors, the staphylococcus gains entrance through the perforated drum, and while acute otitis is usually monomicrobial, the chronic lesions are practically always polymicrobial, and while *Staphylococcus albus* is the organism most frequently present it is usually associated with organisms that may be considered for the most part saprophytic; they attribute chronicity to staphylococcal infection—a view denied by Pes and Gradenigo.⁹⁸ Lermoyez and Helme⁹⁹ reaffirm their belief in staphylococci being the essential agent in the production of chronic otorrhea, and deny that anatomic conditions are of very much importance in the perpetuation of suppuration.

TABLE.*

Staphylococcus in pure culture.....	75
“ with other staphylococci	24
“ “ Pneumococcus	26
“ “ Streptococcus	21
“ “ Proteus vulgaris	7
“ “ Bacillus saprogenes I	7
“ “ Bacillus pyocyaneus	3
“ “ Bacillus pseudoinfluenzae	2
“ “ Bacillus influenzae	2
“ “ Micrococcus tetragenus	1
“ “ Micrococcus versicolor (Flügge)	1
“ “ Bacillus of Friedländer	1
“ “ Proteus vulgaris and Bacillus pyocyaneus	1
“ “ Streptococci and bacilli	2
“ “ Streptococcus and Bacillus pyocyaneus	2
“ “ Streptococcus and nonpathogenic Bacillus	3
“ “ Streptococcus and Pneumococcus	1
“ “ Streptococcus, Pneumococcus, and Bacillus saprogenes I	1
“ “ Streptococcus and Bacillus diphtheriae	8
“ “ Streptococcus, Bacillus striatus albus, Micrococcus liquefaciens albus, Bacillus subtilis, and Sarcina lutea and alba	1
“ “ Streptococcus and Bacillus striatus albus	2
“ “ Streptococcus, Bacillus striatus albus, and torula	1

*The majority of writers on staphylococcal infection note the finding of staphylococci without specifying the type; when the kind of staphylococcus is stated we have usually found that it was either *S. aureus* or *S. albus*, and occasionally *S. citreus*; on account of the confusion of records the naming of any particular form would be confusing, and I have therefore adopted the admittedly objectionable custom.

Staphylococcus with Streptococcus, yellow yeast and unknown bacteria.....	1
“ “ Streptococcus, Bacillus striatus albus, Bacillus tuberculosis, Aspergillus niger, and Penicillium glaucum.....	1
“ “ Streptococcus, Staphylococcus parvulus and Bacillus perfringens.....	1
“ “ Streptococcus, Bacillus striatus albus, and Oldium albicans.....	1
“ “ Streptococcus and Bacillus pyogenes fetidus.....	3
“ “ Streptococcus, Micrococcus fetidus, and unnamed coccus and bacillus.....	1
“ “ Staphylococcus (Irregular) and an unnamed cocobacillus.....	1
“ “ Micrococcus fluidis albus and Micrococcus candicans.....	1
“ “ Micrococcus candicans.....	1
“ “ Bacillus saprogenes, and Pneumococcus	3
“ “ Bacillus striatus albus, Micrococcus liquefaciens albus and Streptococci.....	1
“ “ Bacillus typhosus.....	1
“ “ Bacillus coli communis.....	1
“ “ Proteus vulgaris, Streptobacillus, Micrococcus fetidus.....	1
“ “ Proteus vulgaris, Bacillus radiformis, Bacillus ramosus, Bacillus thetoides, Spirillum nigrum, Bacillus perfringens, 2 unnamed bacilli.....	1
“ “ unidentified bacilli.....	5
“ “ unidentified cocci.....	2
“ “ unidentified diplococci.....	3
Total.....	221
Pyogenic cocci, types not stated but from the context it is evident that the streptococci can be excluded.....	55
Total.....	276

Pneumobacillus of Friedländer.—In literature there are a number of instances showing that the bacillus of Friedländer¹⁰⁰ has been confused with the pneumococcus of Talamon¹⁰¹ and Frankel,¹⁰² which has also been studied by Pasteur, Roux and Chamberland,¹⁰³ and by Sternberg.¹⁰⁴ It has been possible in most instances to determine by the context or by the description to which organism the author referred, and when such differentiation was impossible, the finding has not been included in the statistics given in this article.

Zaufal reports a case in which this organism was identified in the bloody, serous discharge obtained by paracentesis. Weichselbaum¹⁰⁵ found post mortem the bacillus of Friedländer together with nonpathogenic organisms in the purulent secretion of the tympanum, mastoid process, and the edematous fluid of the lung. Chatterlier in 1888 took the ground that this was one of the important organisms in a certain group of otitic inflammations. Kossel has noted the coincidence of Friedländer's organism with the pneumococcus. Blaxall

notes that it is not a frequent factor in scarlatinal lesions. Moos and Netter admit a true primary pneumobacillary otitis. Infection of the middle ear by Friedländer's organism is infrequent, of short duration, subsiding promptly or being prolonged by secondary infection, during the activity of which the pneumobacillus commonly disappears.

TABLE.

Bacillus of Friedländer in pure culture	7
“ “ with nonpathogenic cocci.....	1
“ “ “ Bacillus pseudoinfluenzæ.....	2
“ “ “ staphylococcus	1
Total.....	11

Bacillus Typhosus.—According to observers already quoted the suppurating processes, including otitis media, accompanying typhoid, are due to pyogenic organisms, and not to the typhoid bacillus. Since the work of Orloff¹⁰⁶ supported by the investigations of Gilbert and Girode,¹⁰⁷ the pyogenic powers of the typhoid bacillus have been generally conceded. Lionel de Crevoisier and de Vomecourt observe that up to 1892 the typhoid bacillus had not been found in otitis—a statement that ignores the observation of Destree,⁸⁵ who claimed the identification of the organism in otitic pus. Prochaska⁶⁷ has identified the typhoid bacillus in the purulent complications and Preysing has found it in pure culture in both tympanums in a girl of 16 years dead of typhoid fever; there was a beginning suppurative otitis media. Professor Coplin¹⁰⁸ has observed the typhoid bacillus in suppurative mastoiditis; it was associated with pyogenic cocci. The clinical data are not available.

TABLE.

Bacillus typhosus in pure culture.....	2
“ “ with pyogenic cocci.....	2
Total.....	4

Bacillus Diphtheriæ.—According to Duplay¹⁰⁹ there is a true diphtheritic otitis media, and Moos¹¹⁰ has demonstrated bacteria in the lymphatic space of the semicircular canals, in the aqueduct of the vestibule, and has noted the formation of diphtheritic membrane in the labyrinth. In some cases there was a secondary infection by pyogenic cocci. As in typhoid most observers are clearly of the opinion that otitic complications of diphtheria are due to infection by other organisms. Wendt¹¹¹ and Schwartz¹¹² believe that in its initial stages

inflammation of the middle ear in diphtheria is catarrhal. That the ear is not always involved, even in fatal cases, is shown by the case reported by Kuffer,¹¹³ who found these structures uninvolved even post mortem. Prochaska found diphtheria bacilli associated with pyogenic organisms in otitis media accompanying typhoid fever, although diphtheria bacilli were not found in the throat. Hirsch²⁰ has studied the membrane in the middle ear in which he had found micrococci and cocci arranged in chains. Burekhardt-Merian,¹¹⁴ Loring,¹¹⁵ Moos¹¹⁰ and others have reported similar cases. The diphtheria bacillus has been recognized in discharges of otitis media, by Kossel,¹¹⁶ Kuttcher,¹¹⁷ Councilman,¹¹⁸ Baginsky,¹¹⁹ Wright,¹²⁰ Podack,¹²¹ Burrows,¹²² Stephens and Parfitt.¹²³ In a most careful and elaborate study of 220 fatal cases of diphtheria, Councilman, Mallory and Pearce¹²⁴ record the bacteriologic findings in 68 cases, in only 3 of which was a pure culture of the diphtheria bacillus found.

The following table of collected cases probably falls short of total recorded findings by reason of the fact that a number of observers state that the diphtheria bacillus has been found without giving the number of cases. The organisms with which it is associated have been, usually, the pneumococcus, streptococcus, staphylococcus, and nonpathogenic bacteria.

TABLE.

Diphtheria bacillus in pure culture.....	5
" " associated with other organisms.....	48
Total.....	53

Bacillus of Tuberculosis.—This organism is essentially present only in the more persistent otorrheas. Occasionally a case will be observed in which it may be found early in the disease. In such cases there has usually been a latent tuberculosis which has assumed an acute suppurative activity as the result of some infection engrafted upon a more chronic process. Nathan¹²⁵ found the tubercle bacillus in 12 of 40 cases of suppurative otitis media. Eschle,¹²⁶ Voltolini,¹²⁷ Kanzler¹²⁸ and Haberman,¹²⁹ have identified the tubercle bacillus in tuberculous otitis. Gottstein¹³⁰ and Gessler¹³¹ believe that the tubercle bacillus can always be demonstrated in tuberculous otitis if sufficient material can be obtained, and if the examination is made early in the case. Wolf,

of Frankfort, has called attention to tuberculous necrosis of the ossicles.

TABLE.

Bacillus tuberculosis in pure culture.....	14
“ “ “ with streptococcus.....	5
“ “ “ streptococcus, staphylococcus, Bacillus striatus albus, Aspergillus niger and Penicillium glaucom.....	1
Total.....	20

Bacillus Pyocyaneus.—Most of the references to cases in which *Bacillus pyocyaneus* was found in pure culture have been included in data already given. Martha¹³² and Pes, and Gradenigo¹³³ are also among the observers who have recorded instances of otitis media in which no other organism than *Bacillus pyocyaneus* could be found. As a rule *pyocyaneus* infection is secondary and is usually associated with the presence of other organisms. It is found in chronic cases.

TABLE.

Bacillus pyocyaneus in pure culture.....	13
“ “ “ with Streptococcus.....	2
“ “ “ Bacillus pyogenes fetidus.....	4
“ “ “ Pneumococcus and Bacillus sap- rogenes.....	6
“ “ “ Pneumococcus.....	1
“ “ “ Staphylococcus.....	3
“ “ “ Staphylococcus and Streptococ- cus.....	2
“ “ “ Streptococcus and Spirillum.....	1
“ “ “ Proteus vulgaris and Staphylococ- cus.....	1
“ “ “ Bacillus pseudoinfluenzae.....	1
Total.....	34

Miscellaneous.—It is quite beyond the scope of this paper to consider in detail every organism that has been found in otitis media. Before, however, tabulating the organisms not already mentioned, a few of little more than passing interest may be mentioned. Warnecke¹³⁴ has reported 3 cases of chronic otitis in which the xerosis bacillus was found. A large number of organisms infrequently observed have been recorded by Maggiori and Gradenigo,¹³⁵ and by Edward Rist.⁵³ The last named writer has added what is probably one of the most important contributions to our knowledge of otitis media. His studies were directed particularly to a consideration of the anaërobic organisms present in otitis, mastoiditis, meningitis, and metastases of otitic origin.

He concludes that acute otitis is usually due to the

streptococcus and pneumococcus and other organisms already considered, but that chronic otorrheas are practically always polymicrobial. Among the organisms found in the last named group, are a number of anaërobes, to some of which the fetor, pulmonary gangrene, and arthritic lesions may be attributed. Majocchi¹³⁶ has reported an actinomycotic otitis media, and Valentine¹³⁷ the presence of *Oidium albicans* in otitis media. Invasion of the middle ear by aspergilli probably never occurs in the absence of perforation of the tympanum. After the latter accident, however, numerous forms of mold have been found in the discharges. Minor¹³⁸ reports a case of parasitic otitis in which *Aspergillus flavus* was found.

The following tables include organisms not already tabulated or otherwise recorded in this paper:

TABLE OF MICROCOCCUS TETRAGENUS.

Micrococcus tetragenus in pure culture.....	1
“ “ with Pneumococcus.....	3
“ “ “ Staphylococcus.....	1
“ “ “ other organisms not given, and not included in previous tables.....	3
Total.....	8

TABLE OF BACILLI.

Bacillus acidilactici with Streptococci and saprophytes.....	2
“ coli communis in pure culture.....	4
“ “ “ with Pneumococcus.....	3
“ “ “ “ Streptococcus.....	1
“ “ “ “ Staphylococcus.....	1
“ of influenza in pure culture.....	2
“ “ “ with Staphylococcus.....	2
“ pseudoinfluenzæ in pure culture.....	9
“ “ “ with Pneumococcus.....	10
“ “ “ “ Streptococcus.....	4
“ “ “ “ Staphylococcus.....	2
“ “ “ “ bacillus of Friedländer.....	1
“ “ “ “ Bacillus pyocyaneus.....	1
“ “ “ “ Bacillus perfringens, Bacillus ramosus, a spirochæte, Micrococcus foetidus.....	1
“ pyogenes foetidus “ Streptococcus.....	4
“ “ “ “ Staphylococcus.....	3
“ “ “ “ Bacillus pyocyaneus.....	4
“ perfringens “ Streptococcus, Staphylococ- cus and Staphylococcus parvulus.....	1
“ “ “ “ Staphylococcus, Bacillus ra- difformis, Bacillus ramosus, Bacillus thethoides, Spirillum nigrum, 2 un- named bacilli and Pro- teus vulgaris.....	1
“ “ “ “ Bacillus pseudoinfluenzæ, Bacillus ramosus and a spirochæte, Micrococcus foetidus.....	1

Bacillus radiformis			with Staphylococcus , Bacillus ramosus , Bacillus perfringens , Bacillus thethoides , Spirillum nigrum , Proteus vulgaris , and 2 unnamed bacilli	1
"	ramosus	"	" Staphylococcus , Bacillus radiformis , Bacillus thethoides , Spirillum nigrum , Bacillus perfringens , 2 unnamed bacilli, and Proteus vulgaris	1
"	"	"	" Bacillus pseudoinfluenzae , Bacillus perfringens , Micrococcus foetidus , and a splerochete	1
"	"	"	" Streptococcus , Streptococcus tenuis of Veillon, and an unnamed bacillus.....	1
"	"	"	" Bacillus serpens	1
"	"	"	" an unnamed bacillus.....	1
"	saprogenes I	"	in pure culture.....	1
"	"	"	with Pneumococcus	8
"	"	"	" Bacillus pyocyaneus	8
"	"	"	" Pneumococcus , Staphylococcus , and Streptococcus	1
"	striatus albus	"	" Staphylococcus , Streptococcus , Bacillus subtilis , Micrococcus liquefaciens and Sarcina lutea and alba	1
"	"	"	" Staphylococcus and Streptococcus	2
"	"	"	" Staphylococcus , Streptococcus , and torula	1
"	"	"	" Streptococcus , and Aspergillus niger	1
"	"	"	" Staphylococcus , Bacillus tuberculosis , Aspergillus niger and Penicillium glaucum	1
"	"	"	" Streptococcus , white yeast and unidentified diplococci	1
"	"	"	" Streptococcus , pink yeast and Sarcina lutea	1
"	"	"	" Streptococcus , Staphylococcus , and Oldium albicans	1
"	"	"	" Streptococcus , Staphylococcus and Micrococcus liquefaciens albus	1
Bacillus subtilis			in pure culture.....	1
"	"	"	with Pneumococcus	1
"	"	"	" Streptococcus , Staphylococcus , Micrococcus liquefaciens , Sarcina lutea and alba	1
"	thethoides	"	" Staphylococcus , Bacillus radiformis , Bacillus perfringens , Spirillum nigrum , Bacillus ramosus , Proteus vulgaris , and 2 unnamed bacilli	1
"	vulgaris	"	in pure culture	4
"	"	"	with Staphylococcus	7
"	"	"	" Staphylococcus and Bacillus pyocyaneus	1
"	"	"	" Staphylococcus , Streptobacilli , Micrococcus foetidus , Staphylococcus foetidus , irregular Staphylococcus , and unnamed coccobacilli	1

Bacillus vulgaris

with Staphylococcus, Bacillus ra-
diformis, Bacillus ramosus,
Bacillus thethoides,
Bacillus perfringens, Spirillum
nigrum, and 2 unidentified bacilli

.....	1
Total.....	100

CASES EXAMINED BY DR. FUNKE.

CASE I.—E. H., a boy; aged 6 years. Chronic suppurative otitis media. Patient never had diphtheria or scarlet fever; had measles when 3 years of age. There was slight pain in both ears a year ago, and a few days later they began to discharge. He came to hospital on account of slight deafness. Both tonsils were slightly enlarged; nasopharyngeal catarrh. Bacteria found; pure culture of Staphylococcus pyogenes albus.

CASE II.—H. G., aged 20 years; clerk. Otorrhea of 5 years' duration, coming on without assignable cause. Examination showed the patient thin, anemic, and suffering from persistent cough, profuse mucopurulent expectoration and night sweats; is losing weight rapidly. Bacteria found: Bacillus coli communis and Proteus vulgaris. A careful search failed to demonstrate the presence of tubercle bacilli.

CASE III.—Mrs. A. F., housekeeper; acute otitis media. After an operation about a year ago she began to complain of severe pain in the hypogastric and right iliac regions; this gradually extended to the right shoulder, and from there to the right side of the face and right ear. The pain in the last situation began a week before examination, and was followed in 2 days by profuse discharge; pain continuing. A week later, mastoid was opened. Bacteria found: Pneumococcus and Staphylococcus pyogenes albus.

CASE IV.—W. O., aged 26; bricklayer. Chronic suppurative otitis media which has persisted for 23 years; followed scarlet fever. Bacteria found; pure culture of Staphylococcus pyogenes albus.

CASE V.—L. S., aged 21; teamster. Chronic suppurative otitis media following an attack of scarlet fever at the age of 5 years. Bacteria found: Staphylococcus pyogenes albus, Proteus vulgaris and an unidentified bacillus.

CASE VI.—J. H. R., aged 49 years. Chronic suppurative otitis media. March, 1900, a tumor had been removed from ramus of inferior maxilla; a short time later there was a slight discharge from the right ear, followed in a month by temporal and mastoid pain, and on second day trephining of mastoid. Bacteria found: Bacillus pyogenes foetidus and Proteus vulgaris. The interesting feature of this case is the rapidly developing fetor and the supplanting of the primary instigator of the otitis by the organisms found.

CASE VII.—H. H. T., aged 26 years. Influenza in February, 1900, followed by severe pain in right ear, and a short time later by an abundant yellowish discharge; in April, mastoid became tender and swollen and was opened May 10. Bacteria found: Staphylococci pyogenes albus and aureus.

CASE VIII.—C. B., aged 27; housewife. Chronic suppurative otitis media, alleged to have followed childbirth 5 years ago, since which time it has been continuous. During last 3 weeks slight deafness has appeared. Discharge is horribly fetid. Bacteria found: Staphylococcus pyogenes albus, Micro-

coccus tetragenus, *Bacillus pyogenes fetidus*, and *Aspergillus niger*.

CASE IX.—S. H., aged 24 years; laborer. About 2 months ago he was operated upon for removal of a cystic tumor of the frontal sinus. Just prior to the operation both ears began to suppurate without any apparent cause other than the tumor. Bacteria found: *Staphylococci pyogenes albus* and *aureus*.

CASE X.—A. C., aged 27; motorman. Chronic suppurative otitis media of 15 years' duration; followed scarlet fever; considerable deafness. Bacteria found: *Staphylococci pyogenes albus* and *aureus*, and an unidentified bacillus.

CASE XI.—D. E., aged 16; single. For 8 years she has experienced some difficulty in breathing, which is much aggravated when she has a cold. Upon examination enlarged turbinate bones and a granular inflammation of the postnasal space were found. About 2 weeks ago she experienced a slight pain in both ears, but this soon ceased and they both began to discharge a dirty white or yellowish white secretion. Bacteria found: *Staphylococcus pyogenes albus*; *Bacillus diphtheriæ* and *Bacillus pseudodiphtheriæ*.*

CASE XII.—A. P., aged 41; tailor. Influenza complicated by bilateral suppurative otitis media, April 1; 20 days later double mastoiditis. Pus from the ear and mastoid was examined May 15. Bacteria found: *Staphylococcus pyogenes aureus* and *pseudodiphtheria bacillus*.

CASE XIII.—F. B., aged 34; housewife. Bilateral suppurative otitis media persisting since an attack of scarlet fever during childhood; aggravated since an attack of influenza in December, 1899; rightsided mastoiditis February 4, 1900; mastoid trephined February 11, 1900. Bacteria found: *Staphylococcus pyogenes albus*.

CASE XIV.—J. B., aged 15. Chronic suppurative otitis media; no evident cause; fetor. Bacteria found: *Bacillus pyogenes fetidus*; *Proteus vulgaris* and a bacillus that resembles the colon bacillus, but does not turn litmus, is nonmotile and nonpathogenic.

CASE XV.—R. C., aged 19; cigarmaker. Chronic suppurative otitis media of 11 years' duration; followed measles. Bacteria found: *Bacillus pyocyaneus* and an organism resembling the *Bacillus tuberculosis*, but not obtained in cultures.

CASE XVI.—F. McC., aged 5 years. Acute otitis media following scarlet fever and diphtheria. The larger joints are painful. Bacteria found: *Staphylococcus pyogenes aureus* and a *Diplococcus* much larger than the ordinary pus cocci, not encapsulated, did not stain by Gram's method, and was not obtained in cultures.

CASE XVII.—J. M., aged 44; waiter. Chronic suppurative otitis media, consecutive to repeated attacks of coryza. Bacteria found: *Bacillus subtilis* and *Bacillus acidi lactici*.

CASE XVIII.—E. T., aged 37; physician. Chronic suppurative otitis media of 32 years' duration; followed trauma. Bacteria found: *Bacillus coli communis* and a bacillus resembling that found in Cases V and XV.

CASE XIX.—W. H., aged 26; cigarmaker. Chronic suppurative otitis media since childhood. The patient had measles, diphtheria, scarlet fever and acute articular rheumatism, but

*The organism designated in this paper "*pseudodiphtheria bacillus*" corresponds in morphology, tinctorial reactions, virulence, etc., to that described by Hewlett and Knight,¹³⁹ and is probably but a modified form of the true *diphtheria bacillus*.

does not recall that the present condition can be traced to any of these. Bacteria found: *Bacillus diphtheriæ* and *Bacillus pyocyaneus*.

CASE XX.—C. A., aged 22. Chronic suppurative otitis media of 8 months' duration. Cause not known. Has atrophic rhinitis and pharyngitis. Bacteria found: *Bacillus pyocyaneus* in pure culture.

CASE XXI.—R. S., aged 8. Chronic suppurative otitis media, which probably followed an attack of influenza a year ago. Bacteria found: *Staphylococcus pyogenes albus* and *Bacillus pyocyaneus*.

CASE XXII.—T. C. R., aged 16; clerk. Chronic suppurative otitis media. Patient is thin, anemic, has cough of a year's duration. Bacteria found: *Staphylococcus pyogenes albus* and *Bacillus pyocyaneus*.

CASE XXIII.—M. S., aged 7; female. Chronic suppurative otitis media; duration 3 years; cause not known. Bacteria found: pure culture of *Staphylococcus pyogenes albus*.

CASE XXIV.—M. H., aged 10. Chronic suppurative otitis media due to an associated pharyngeal and nasopharyngeal catarrh. Otitic complication has persisted for a year. Bacteria found: *Staphylococcus pyogenes albus*; *Bacillus coli communis*, and a bacillus identical with that observed in Cases V, XV, XVIII.

CASE XXV.—L. H., aged 3 years. Acute otitis media; clinical cause not determined. Nose and nasopharynx normal. Bacteria found: *Staphylococci pyogenes albus* and *aureus*.

CASE XXVI.—A. R., aged 11. Chronic suppurative otitis media of 4 years' duration; fetid; followed diphtheria. Bacteria found: a nonpathogenic *Diplococcus* and *Bacillus pyogenes fetidus*.

CASE XXVII.—R. G., aged 10. Chronic suppurative otitis media; duration 1 year; followed diphtheria. Bacteria found: *Staphylococcus pyogenes albus*, *Sarcina citrina* and an unidentified bacillus that did not stain by Gram's method, and was not obtained in cultures.

CASE XXVIII.—A man of 26. Chronic suppurative otitis media. The patient has been under observation at the clinic since 1892, at which time one mastoid was opened to curet the mastoid cells and antrum that had undergone suppuration consecutive to an otorrhea that was probably of tuberculous origin. Some time later the other mastoid began to suppurate, necessitating an operation upon it; but the otorrhea continued, and in November, 1899, another operation was performed upon the right mastoid. The pus is said to have been examined at the time of the second operation and the tubercle bacillus found. Nevertheless both ears continued to discharge while the operation relieved the symptoms of mastoid disease. In the latter part of May, 1900, I examined the secretion from the ears and found the *Proteus vulgaris* (Hauser). The otorrhea continued, and in the latter part of September, 1900, he began to suffer severe pain in the right ear, mastoid process and the side of the head. The mastoid was again opened and curetted; the condition rapidly subsided, suppuration ceased. The pus was not examined at the time of the last operation. About January 1, 1901, the left ear, mastoid and the left side of the head became extremely painful. This mastoid was opened and curetted; this relieved all symptoms as well as the suppuration, and up to the present time both ears and mastoids have been free from suppuration. Bacteria found: *Proteus vulgaris* and *Bacillus pyo-*

cyaneus. Since the *Proteus vulgaris* was present in both ears when I examined the pus, in the latter part of May, 1900, and when the acute symptoms supervened in the left ear and mastoid process there was an additional microorganism, it is highly probable that the acute exacerbation was due to *Bacillus pyocyaneus*.

CASE XXXIX.—B. V., aged 8. Chronic suppurative otitis media, bilateral, 4 years' duration; postnasal adenoids. Bacteria found: *Bacillus saprogenes* I, and an unidentified bacillus.

CASE XXX.—K. J., aged 3. Acute suppurative otitis media following measles. Bacteria found: *Staphylococcus pyogenes albus* and *Pneumococcus*.

CASE XXXI.—R. O., aged 7. Chronic otitis media; duration 1 year; followed measles; beginning mastoiditis for which trephining was done. Bacteria found: *Staphylococcus pyogenes aureus* and *Bacillus diphtheria*.

CASE XXXII.—W. H., aged 6. Chronic suppurative otitis media, bilateral; large mass of postnasal adenoids. Ear discharge is fetid. Bacteria found: *Staphylococcus pyogenes albus*, *Bacillus pyogenes fetidus*, and *Bacillus saprogenes* I.

CASE XXXIII.—W. W., aged 24; bricklayer. Chronic suppurative otitis media, bilateral; duration 3 months; followed influenza. Bacteria found: *Staphylococcus pyogenes albus*, pink yeast, and *Bacillus pyocyaneus*.

CASE XXXIV.—C. D., aged 3 years. Chronic suppurative otitis media, bilateral; duration 2 months; followed measles. Bacteria found: *Staphylococcus pyogenes albus* and *Bacillus subtilis*.

CASE XXXV.—F. S., aged 4. Acute suppurative otitis media, unilateral; suppurative mastoiditis. Bacteria found: *Streptococcus pyogenes* and *Bacillus diphtheria*.

CASE XXXVI.—E. D., aged 41, farmer. Chronic suppurative otitis media, right ear; followed injury received 2 years ago; mastoiditis. Mastoid was opened and cureted. Bacteria found: *Pneumococcus* and *Bacillus diphtheria*.

CASE XXXVII.—C. R., aged 3. Acute otitis media, bilateral; followed scarlet fever. Bacteria found: *Streptococcus pyogenes* and *Bacillus pseudodiphtheria*.

CASE XXXVIII.—O. C., aged 4 years. Chronic otitis media, bilateral; duration 2 months; followed scarlatina. Bacteria found: *Staphylococcus pyogenes albus* and *Sarcina citrina*.

CASE XXXIX.—S. G., aged 64, liquor dealer. Acute suppurative otitis, unilateral; followed influenza. Mastoiditis. Mastoid was opened and cureted. Bacteria found: *Staphylococcus pyogenes aureus*.

CASE XL.—A. F., aged 3. Chronic otitis media with mastoiditis; duration 5 months; mastoid opened 6 weeks after onset. Bacteriologic examination 3½ months later. Bacteria found: *Staphylococcus pyogenes albus* and *Proteus vulgaris*.

CASE XLI.—A. C., aged 10. Chronic suppurative otitis media and mastoiditis of 5 years' duration; followed mixed infection of scarlatina, measles and diphtheria. Pus greenish. Bacteria found: *Bacillus pyocyaneus* and *Bacillus saprogenes* I.

CASE XLII.—A male; adult. Chronic suppurative otitis media. Operation for mastoiditis; other clinical data misplaced. Bacteria found: *Staphylococcus pyogenes albus* and *Proteus vulgaris*.

CASE XLIII.—M. O., aged 14. Chronic suppurative otitis media; duration 2 years. Cause not determined; anemia.

Nose and throat negative. Bacteria found: *Staphylococcus pyogenes albus*, *Bacillus pyogenes foetidus*, and *Bacillus saprogenes* I. Careful search failed to demonstrate the presence of the tubercle bacillus.

CASE XLIV.—Chronic suppurative otitis media. Patient of Dr. Solt, who failed to obtain the clinical data. Bacteria found: *Staphylococcus pyogenes albus*, *Bacillus pyocyaneus*, *Bacillus saprogenes* I.

CASE XLV.—A. C., aged 4. Acute suppurative otitis media, bilateral; followed scarlet fever. Bacteria found: *Pneumococcus*, *Staphylococcus cereus albus* and *pseudodiphtheria* bacillus.

CASE XLVI.—B. C., aged 2; male. Acute otitis media, bilateral; followed scarlatina. Bacteria found: *Bacillus* of Friedländer, and *Bacillus xerosis*.

CASE XLVII.—R. T., aged 5. Acute otitis media, bilateral; followed scarlet fever. Bacteria found: *Pneumococcus* and *Staphylococcus cereus albus*.

CASE XLVIII.—D. P., aged 5; male. Acute suppurative otitis media, bilateral; followed scarlatina. Bacteria found: *Streptococcus pyogenes*, *Staphylococcus cereus albus* and *Sarcina citrina*.

CASE XLIX.—D. G., aged 4; male. Acute suppurative otitis media, bilateral; followed scarlatina. Bacteria found: *Pneumococcus*, *Staphylococcus pyogenes albus*, *Bacillus pseudodiphtheriae*, and *Saccharomyces albicans*.

CASE L.—E. M., aged 30; china-packer. Chronic suppurative otitis media, fibrinous meningitis (cerebral and spinal), pulmonary edema, parenchymatous nephritis. The pneumococcus had been demonstrated in the cerebrospinal fluid during life, and a few of these organisms were found in sections of the meninges, and in spreads made post mortem. There was no gross path of infection that could be identified between the ear and the meninges. Bacteria found: the middle ear yielded a pure culture of the *Staphylococcus pyogenes albus*; the ethmoidal sinuses and the auditory nerve, *Staphylococcus pyogenes aureus*, *Bacillus coli communis*, *Sarcina citrina* and pink yeast.

CASE LI.—A. V., aged 44; fish dealer. Acute suppurative otitis media. January 7 the patient had an attack of influenza; on the eighth, pain in left ear; on ninth, the drumhead ruptured; on tenth, there was edema over the mastoid; on twelfth, mastoid opened. Bacteria found: at the time the mastoid was opened a pure culture of *Streptococcus pyogenes*; 3 weeks later the *Staphylococcus pyogenes albus* were abundantly present, while *Streptococcus pyogenes* was isolated with difficulty.

CASE LII.—A. T., aged 6; male. Acute suppurative otitis media; cause undetermined. Patient had mastoiditis. Bacteria found: pus in the canal, pus over mastoid and inoculations from the mastoid cells yielded *Staphylococcus pyogenes albus*. Anaerobic cultures were negative, except for this organism.

CASE LIII.—M. C., aged 23; nurse. Acute suppurative otitis media; followed acute coryza. Bacteria found: *Pneumococci* in pure culture.

CASE LIV.—P. J. D., aged 28; bricklayer. Acute suppurative otitis media, following coryza. Inoculations a week after rupture of drumhead. Bacteria found: *Pneumococcus* and *Staphylococcus pyogenes albus*.

CASE LV.—Infant, aged 1 month. Acute otitis media (sup-

purative); cause undetermined. Bacteria found: *Bacillus diphtheriæ*, *Bacillus pseudodiphtheriæ*, and *Bacillus pyogenes foetidus*.

CASE LVI.—J. F., aged 22; cigarmaker. Acute suppurative otitis media, associated with influenza. Bacteria found: *Streptococcus pyogenes*, and *Staphylococcus pyogenes albus*.

CASE LVII.—G. H., aged 49; laborer. Acute suppurative otitis media, bilateral. There was a profuse fetid discharge. Bacteria found: *Bacillus pyogenes foetidus*.

CASE LVIII.—M. C., aged 23; nurse. Acute otitis media following influenza. Operation performed for mastoiditis. Bacteria found: pure culture of *Streptococcus pyogenes*.

CASE LIX.—W. B. M., aged 15; elevator boy. Acute suppurative otitis media, bilateral. Clinical cause undetermined. Bacteria found: pure culture of *Bacillus pyocyaneus*.

CASE LX.—G. G., aged 5; female. Chronic suppurative otitis media due to adenoids. Bacteria found: *Staphylococcus pyogenes albus* and *Proteus vulgaris*.

CASE LXI.—L. B., aged 6. Acute otitis media, suppurative, unilateral; followed influenza. Bacteria found: cultures revealed only the *Staphylococcus pyogenes aureus*. In spreads there are a few bacilli possessing morphologic and tinctorial characters of the influenza bacillus. As this organism was not found in any of the cultures, and as no cultures were made on hemoglobin-containing mediums, the negative finding becomes of value.

The influenza bacillus was found once in 9 cases consecutive to grip, but at least a week elapsed between the onset of the otitis and the beginning of the discharge in in each case.

Barrett,¹⁴⁰ in an article on acute suppurative otitis media following influenza, states that the *Bacillus influenzae* is pyogenic. The writer has been unable to find any other statement corroborating this view, but, this is supported by the findings of Bulling,⁸⁸ who demonstrated the *Bacillus influenzae* twice in pure cultures in cases of acute otitis media following influenza. Scheibe,⁴⁸ who examined 8 cases of acute otitis media, found bacilli in coverglass spreads that did not grow on ordinary culture mediums, and retained Gram's stain. These bacilli may have been anærobic, yet it is possible that they were influenza bacilli.

With regard to their staining by Gram's method, Kramer, quoted by Barrett, states that they are quite resistant to Gram's fluid when grown in an atmosphere of hydrogen. In 3 of Scheibe's cases the spreads were obtained at the initial paracentesis, and there is every reason to believe that this condition affords an environment as nearly anærobic as is observed in many cases of tetanus.

Tuberculous Otitis.—In addition to the 61 cases reported in detail, I collected 15 cases in which the condi

tion observed, the clinical history and the complications, all justified the diagnosis of tuberculous otitis. It is not deemed necessary to give the clinical history in detail, but it is sufficient to say that each case presented an evident tuberculosis of some part of the body; in most of the cases tuberculosis of the lung was established, some had spinal caries, others tuberculous joints. Careful and repeated examinations were made for the tubercle bacillus, and in one of the most typical cases, inoculation experiments—all with negative results. These cases are not included in the following tables.

CASES EXAMINED.

	Acute.	Chronic.	Total.		Acute.	Chronic.	Total.
Males.....	18	25	41	Unilateral,	10	6	16
Females..	8	12	20	Bilateral ...	14	31	45
	<u>24</u>	<u>37</u>	<u>61</u>		<u>24</u>	<u>37</u>	<u>61</u>
Total.....	24	37	61	Total.....	24	37	61
Cases complicated by mastoiditis.....					7	8	15
Cases consecutive to scarlet fever.....					7	5	12
“ “ “ measles and							
diphtheria (combined).....						1	1
Cases consecutive to diphtheria.....						2	2
“ “ “ measles.....					2	4	6
“ “ “ influenza.....					7	2	9
“ “ “ pharyngeal catarrh.....						4	4
“ “ “ adenoids.....						3	3
“ “ “ tumors.....						2	2
“ “ “ injury.....						2	2
“ “ “ acute coryza.....					3		3
“ “ “ rheumatism.....					1		1
“ “ “ bathing.....						1	1
“ “ “ tuberculosis (?).....						2	2
Unassignable or undetermined.....					4	9	13
	<u>—</u>	<u>—</u>	<u>—</u>		<u>—</u>	<u>—</u>	<u>—</u>
Total.....	24	37	61		24	37	61

BACTERIA FOUND.

Pneumococcus in pure culture.....	1		1
“ and Staphylococcus pyogenes albus.....	3		3
“ “ Staphylococcus pyogenes albus, Bacillus pseudodiphtherie, Saccharomyces albicans.....	1		1
“ “ Staphylococcus cereus albus.....	1		1
“ “ Staphylococcus cereus albus and Bacillus pseudodiphtherie.....	1		1
“ “ Bacillus diphtherie.....		1	1
	<u>—</u>	<u>—</u>	<u>—</u>
Total.....	7	1	8

	Acute.	Chronic.	Total.
Streptococcus pyogenes in pure culture.....	2		2
“ “ “ and Bacillus diphtheriae.....	1		1
“ “ “ Bacillus pseudodiphtheriae.....	1		1
“ “ “ Staphylococcus pyogenes albus.....	1		1
“ “ “ Staphylococcus cereus albus and Sarcina citrina.....	1		1
Total.....	6	—	6
Staphylococcus pyogenes albus in pure culture.....	3	5	8
Staphylococcus pyogenes albus and pneumococcus.....	3		3
Staphylococcus pyogenes albus and pneumococcus, pseudodiphtheria bacillus and Saccharomyces albicans.....	1		1
Staphylococcus pyogenes albus and streptococcus.....	1		1
Staphylococcus pyogenes albus and Staphylococcus pyogenes aureus, and unidentified bacilli.....		1	1
Staphylococcus pyogenes albus, Bacillus diphtheriae and Bacillus pseudodiphtheriae.....		1	1
Staphylococcus pyogenes albus and Bacillus pyocyaneus.....		2	2
Staphylococcus pyogenes albus and Bacillus pyocyaneus and Bacillus saprogenes I.....		1	1
Staphylococcus pyogenes albus and Bacillus coli communis and unidentified bacilli.....		1	1
Staphylococcus pyogenes albus and Bacillus pyogenes foetidus and Bacillus saprogenes.....		2	2
Staphylococcus pyogenes albus and Bacillus subtilis.....		1	1
Staphylococcus pyogenes albus and Sarcina citrina and unidentified bacilli.....		1	1
Staphylococcus pyogenes albus and Sarcina citrina.....		1	1
Staphylococcus pyogenes albus and Saccharomyces roseaceus and Bacillus pyocyaneus.....		1	1
Staphylococcus pyogenes albus and Proteus vulgaris.....		3	3
Staphylococcus pyogenes albus and Proteus vulgaris and unidentified bacilli.....		1	1
Staphylococcus pyogenes albus and Staphylococcus pyogenes aureus.....	2	1	3
Staphylococcus pyogenes albus and Micrococcus tetragenus, Bacillus pyogenes foetidus and Aspergillus niger.....		1	1
Total.....	10	23	33
Staphylococcus pyogenes aureus in pure culture.....	1		1
Staphylococcus pyogenes aureus and Staphylococcus pyogenes albus.....	2	1	3
Staphylococcus pyogenes aureus and Bacillus diphtheriae.....		1	1
Staphylococcus pyogenes aureus and Bacillus pseudodiphtheriae.....	1		1
Staphylococcus pyogenes aureus and Bacillus influenzae.....	1		1
Staphylococcus pyogenes aureus and unidentified bacilli.....	1		1
Staphylococcus pyogenes aureus and unidentified diplococcus.....	1		1
Total.....	7	2	9

	Acute.	Chronic.	Total.
Staphylococcus cereus albus, pneumococcus and Bacillus pseudodiphtheriæ.....	1		1
Staphylococcus cereus albus and pneumococcus.....	1		1
Staphylococcus cereus albus, Streptococcus and Sarcina citrina.....	1		1
Total.....	3		3
Bacillus diphtheriæ and pneumococcus.....		1	1
“ “ “ Staphylococcus pyogenes albus and Bacillus pseudodiphtheriæ.....		1	1
“ “ “ Staphylococcus pyogenes aureus.....		1	1
“ “ “ Bacillus pseudodiphtheriæ and Bacillus pyogenes foetidus.....	1		1
“ “ “ Bacillus pyocyaneus.....		1	1
Total.....	1	4	5
Bacillus pseudodiphtheriæ and Staphylococcus pyogenes albus, pneumococcus and Saccharomyces albicans.....	1		1
Bacillus pseudodiphtheriæ and Staphylococcus pyogenes albus, and Bacillus diphtheriæ.....		1	1
Bacillus pseudodiphtheriæ and Staphylococcus pyogenes aureus.....	1		1
Bacillus pseudodiphtheriæ and Staphylococcus cereus albus and Bacillus pseudodiphtheriæ.....	1		1
Bacillus pseudodiphtheriæ and Streptococcus pyogenes.....	1		1
Bacillus pseudodiphtheriæ and Bacillus diphtheriæ and Bacillus pyogenes foetidus.....	1		1
Total.....	5	1	6
Bacillus pyocyaneus in pure culture.....	1	1	2
“ “ “ and Staphylococcus pyogenes albus.....		1	1
“ “ “ Staphylococcus pyogenes albus and Saccharomyces rosaceus.....		1	1
“ “ “ Bacillus diphtheriæ.....		2	2
“ “ “ Bacillus saprogenes I.....		1	1
“ “ “ Bacillus saprogenes I and Staphylococcus pyogenes albus.....		1	1
“ “ “ Proteus vulgaris.....		1	1
“ “ “ unidentified bacilli.....		1	1
Total.....	1	9	10
Bacillus coli communis and Staphylococcus pyogenes albus and unidentified bacilli.....		1	1
Bacillus coli communis and Proteus vulgaris.....		1	1
Bacillus coli communis and unidentified bacilli.....		1	1
Total.....		3	3
Bacillus pyogenes foetidus in pure culture.....	1		1
Bacillus pyogenes foetidus and Staphylococcus pyogenes albus, Micrococcus tetragenus, Aspergillum niger.....		1	1
Bacillus pyogenes foetidus and Bacillus diphtheriæ and Bacillus pseudodiphtheriæ.....	1		1
Bacillus pyogenes foetidus and Bacillus saprogenes I.....		1	1

	Acute. Chronic. Total.	
<i>Bacillus pyogenes fetidus</i> and <i>Bacillus sapro-</i> <i>genes</i> I and <i>Staphylococcus pyogenes</i> al- bus.....	1	1
<i>Bacillus pyogenes fetidus</i> and <i>Proteus v. nigra</i> . <i>Bacillus pyogenes fetidus</i> and <i>Proteus vulgaris</i> and unidentified bacilli.....	1	1
<i>Bacillus pyogenes fetidus</i> and unidentified coc- cus.....	1	1
Total.....	2	3
<i>Bacillus saprogenes</i> I and <i>Staphylococcus pyo-</i> <i>genes</i> albus and <i>Bacillus pyocyaneus</i>	1	1
<i>Bacillus saprogenes</i> I and <i>Staphylococcus pyo-</i> <i>genes</i> albus and <i>Bacillus pyogenes fetidus</i> . <i>Bacillus saprogenes</i> I and <i>Bacillus pyocyaneus</i> . <i>Bacillus saprogenes</i> I and <i>Bacillus pyogenes</i> <i>fetidus</i>	1	1
<i>Bacillus saprogenes</i> I and unidentified bacillus..	1	1
Total.....	5	3
<i>Bacillus subtilis</i> and <i>Staphylococcus pyogenes</i> albus.....	1	1
<i>Bacillus subtilis</i> and <i>Bacillus acidilactici</i>	1	1
Total.....	2	2
<i>Bacillus influenzae</i> and <i>Staphylococcus pyogenes</i> aureus.....	1	1
Total.....	1	1
<i>Bacillus xerosis</i> and <i>Bacillus Friedländer</i>	1	1
Total.....	1	1
<i>Bacillus acidilactici</i> and <i>Bacillus subtilis</i>	1	1
Total.....	1	1
<i>Sarcina citrina</i> and <i>Staphylococcus pyogenes</i> albus.....	1	1
<i>Sarcina citrina</i> and <i>Staphylococcus pyogenes</i> albus and unidentified bacilli.....	1	1
<i>Sarcina citrina</i> and <i>Staphylococcus cereus</i> albus and streptococcus.....	1	1
Total.....	1	3
<i>Saccharomyces rosaceus</i> and <i>Staphylococcus</i> <i>pyogenes</i> albus and <i>Bacillus pyocyaneus</i> ...	1	1
<i>Saccharomyces albicans</i> and <i>Pneumococcus</i> , <i>Staphylococcus pyogenes</i> albus and <i>Bacil-</i> <i>lus pseudodiphtheriae</i>	1	1
Total.....	1	2

CONCLUSIONS.

The following conclusions are based on a study of the literature of otitis media and my observations:

1. There is no specific organism of otitis media.
2. Acute otitis media is not invariably monomicrobial as is commonly held. The pathogenic organism present may be alone, but with it are frequently found a varying

number of associated bacteria which may or may not be influential in determining the outcome of the case.

3. The organisms commonly found, in the order of frequency, are: The pneumococcus, streptococcus, pyogenic staphylococci (albus and aureus) and bacillus of Friedländer. I am strongly inclined toward the belief in a definite grippal otitis, primarily due to the influenza bacillus, which, however, becomes quickly associated with, or replaced by other organisms.

4. The *Bacillus diphtheriæ* is more commonly present in otorrhea than is usually believed; it may be (a) the initial infecting agent, (b) it may enter with the streptococcus or pneumococcus, or (c) it may be a secondary infection carried to the already infected ear by the fingers of the patient or otherwise, as held by Baginsky.

5. It is reasonable to believe, as my observations show, that it persists for a varying period of time in the discharges, and may constitute a center of danger just as has been thoroughly established concerning its prolonged residence in the nasal cavities, pharynx, etc. Its frequent association with *Bacillus pseudodiphtheriæ* has here the same significance as elsewhere, a factor not as yet fully determined.

6. The streptococcal infections are more grave and persist longer than pure pneumococcal infections, but both are usually supplanted by the staphylococci sooner or later.

7. There is a true pneumobacillary otitis usually acute and quickly converted into a mixed infection. The gravity of the process depends almost exclusively upon the character of the mixed or secondary infection.

8. Chronic suppurative otitis media is practically always a sequence of the acute.

9. Like the acute it possesses no specific organism.

10. Unlike the acute it is practically always polymicrobial.

11. Its polymicrobial character may be evinced in any of 3 ways: (a) A mixed infection of pathogenic organisms; (b) one or more recognized pathogenic organisms (usually pyogenic staphylococci) with one or more bacteria usually regarded as saprophytes; (c) the usual pyogenic and pathogenic bacteria are absent, and the discharges are maintained through the activity of organisms that commonly lead a saprophytic existence.

12. While anaerobic organisms may play an important part in the pathogenesis of chronic suppurative otitis media, my observations have not established their almost constant presence as maintained by Rist.⁵⁵

13. The fetor met in the cases here reported can be explained by the presence of *Bacillus pyogenes foetidus* without anaerobic organisms.

14. All clinical and collated bacteriologic data indicate that otitic inflammations present different bacteriologic findings in different localities. According to Moos,¹¹ during the influenza epidemic of 1890, the otitic complications were due to the pneumococcus in Vienna (Weichselbaum), and to the streptococcus in Strassburg, in Griefswald and in Bonn (Ribbert).

15. Reports gathered from literature establish the existence of a primary tuberculous otitis, but all observers are of one mind as to the almost utter impossibility of routine demonstration of the bacillus in the discharge.

16. For the demonstration of the tubercle bacillus in suspected cases I would recommend the examination of tissue obtained by the curet.

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PARESIS.

A CLINICAL STUDY OF ONE HUNDRED AND FORTY-NINE CASES OCCURRING AT THE PHILADELPHIA HOSPITAL.

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of Philadelphia.

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The science of psychiatry has been largely re-written in the past hundred years; and it is a striking paradox, that the one form of mental disease unknown at the beginning of the last century, is to-day the best understood of all, both clinically and pathologically, and is, as I have remarked in another place, the one unquestioned clinical form of insanity. The mania, melancholia, dementia and idiocy of Pinel might be likened to mere waves on the surface of the mind,—the conception of paresis as a distinct entity being the first successful sounding to any depth in the sea of psychiatry. It may be that in dementia praecox, as presented by Kraepelin, we are again reaching bottom; but however that may be, it suggests a comment that the shifting of views and the changing classification in mental medicine are not a reproach to it, but come from seeing various new outlines of things in an ever-growing light.

While to Bayle is rightly accredited the first pronouncement of the entity of paresis, yet it is a question whether Esquirol did not comprehend the disease more nearly in the modern way, for he insisted that paralysis may be associated with any form of delusion—may “complicate” mania, melancholia (lypomania), as well as ambitious monomania, but

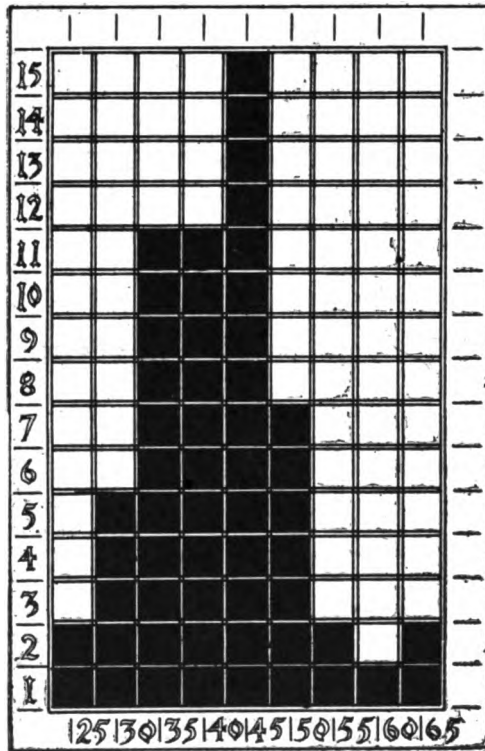


CHART III.

Classic Type of Paresis; 56 cases—both sexes.
The figures at the bottom represent the ages; those at the side the number of cases.

more often the last; and he recognized a type without delusions. Bayle, it appears, made the delusion of grandeur the "necessary symptom" of general paralysis, and how wide of the mark that was, may be learned from Mendel's recent assertion that "two-thirds of the cases of paresis are of the simple demented form."

This statement of Mendel's is somewhat startling, but a glance at our charts 3, 4 and 5, will show that

in Blockley the cases of simple demented form, or "simple form", as I, with the acquiescence of Dr. Dercum, propose to call the form without delusion, are at least more numerous than those of the classic type (65 to 56); a state of things which doubtless would have been astonishing in that institution twenty years ago, and which is particularly interest-

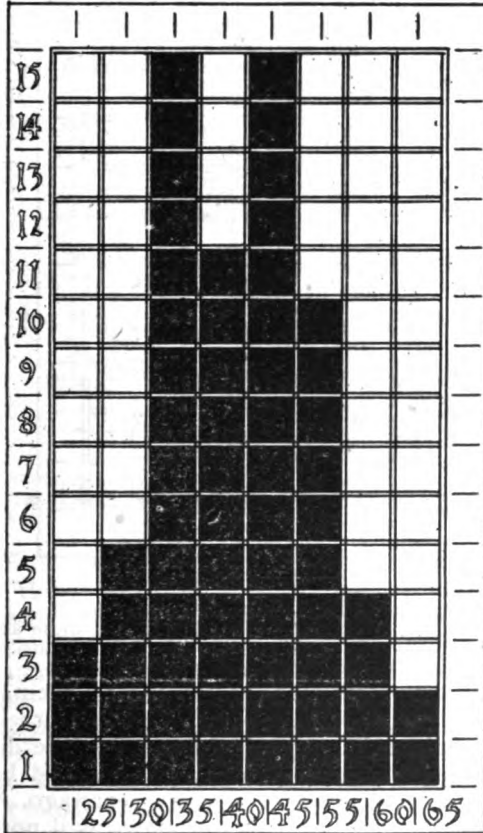


CHART IV.

Demented or Simple Type of Paresis. 65 cases—both sexes.
The figures at the bottom represent the ages; those at the side the number of cases.

ing in view of the wide-spread belief that the type of paresis is changing—that the simple form is growing in numbers—a belief entertained by D. E. Hughes. Again, in charts 1 and 2 we see a proportion of women to men (36 to 113) which is higher than in most of the older statistics; but that paresis is on the increase in women cannot be deduced from these statistics any more than the alleged increase

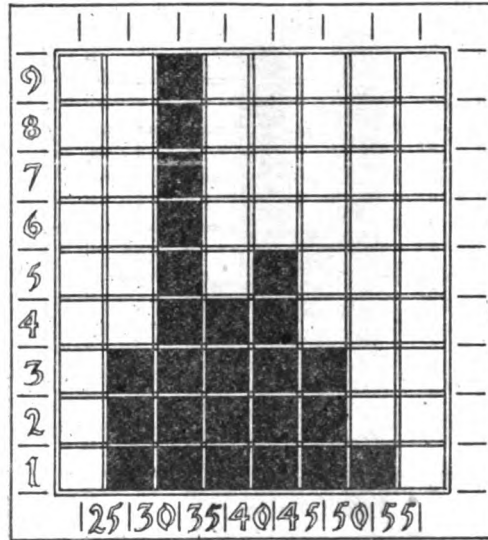


CHART V.

Depressed Type of Paresis: 25 cases—both sexes.
The figures at the bottom represent the ages; those at the side the number of cases.

of the simple form can be established by them. In truth, it is likely that the change is in ourselves more than in the disease; we are making the diagnosis of paresis to-day in cases which would have been called something else not many years ago. And while Mendel's statement quoted above will not be accepted without protest, yet it is doubtless a tack towards the true course, for it is probable that doctors in general are not sufficiently aware of the fact

that *paresis without delusion is exceedingly common*. Too long we have been guiding ourselves by that old idea of Bayle's, that the delusion of grandeur is the "essential symptom" of paresis.

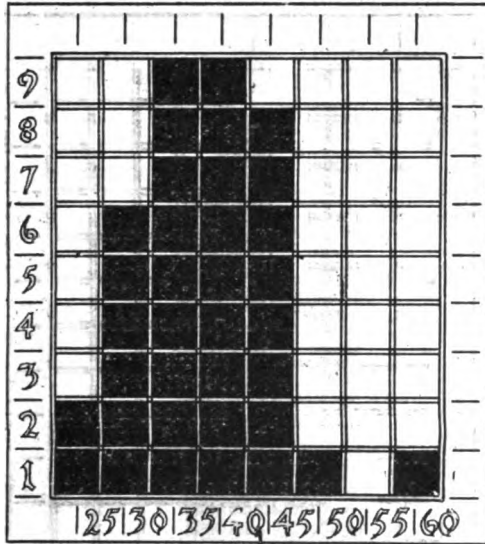


CHART I.

Women—36 Cases.

The figures at the bottom represent the ages; those at the side the number of cases.

Still this curious tendency of the disease is shown in the fact (table No. I) that 21 of our simple cases and 6 of the depressed had at some period a momentary kindling or slow smoldering of the delusion of grandeur; thus case No. 39, bedfast for some months, but aroused at the sight of a new patient struggling with the attendant, got out of bed as if to rescue his fellow patient, exclaiming, "I am the king!"—the only spark of exaltation he ever revealed; and case No. 71, a depressed man, several times amid his lamentations spoke of sums of money and fine clothes which he had at home—statements which we were able to disprove entirely.

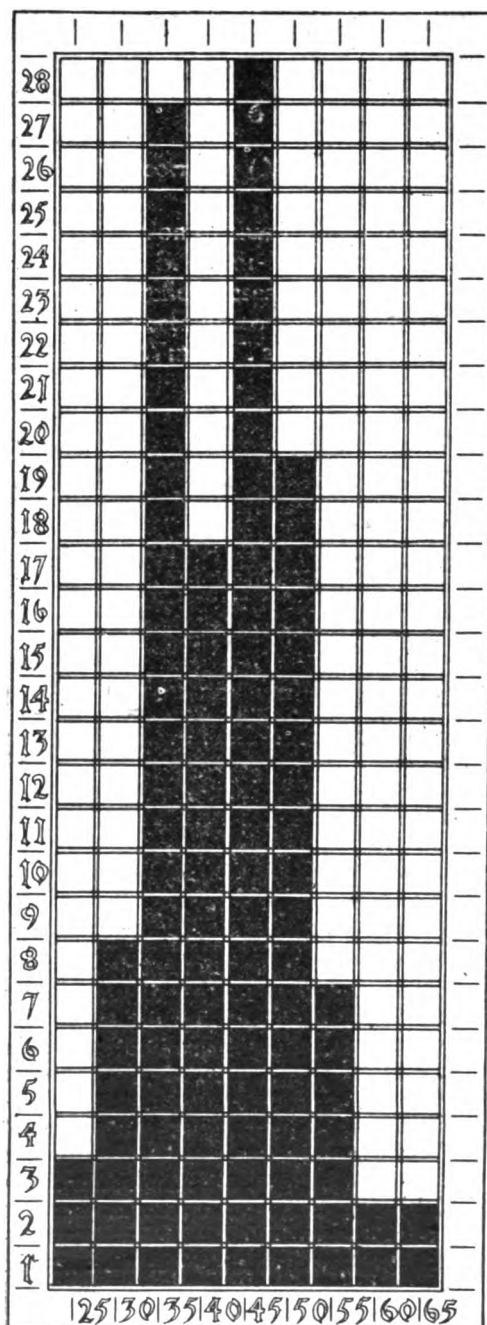


CHART II.

Men—113 cases.
 The figures at the bottom represent the ages; those at the side the number of cases.

TABLE No. I.

Personal histories in the several forms of Paresis with Symptomatology.

	Classic.		Demented.		Depressed.	
	Men	Women	Men	Women	Men	Women
Alcoholic	26	5	27	2	6	2
Addicted to Morphine . .	2	2				
Always eccentric	6	1	4	2	1	1
Head Injury	8		2			
Sunstroke			1			
Past Epilepsy	1	1	1			
Wandering from home . .	8	10	17	7	1	8
Homicidal	9	1	12	2		
Suicidal	4	2	4	3	4	4
Pyromania	2	1	3	1		2
Delusions of Persecution	6	3	2	4	5	3
Delus. Hypochon.	1	1	2	2	1	4
Delus. Grandeur	42	14	15	6	4	2
Delus. Pregnancy		5		5		
Hallucinations of Hearing	3	4	5	6	1	4
Hallucinations of Sight .	2	1			1	1
Hallucinations S. and H.	5	2	7	2	2	5
Aphonia	1		1			
Echolalia	1			1		
Aphasia	1		1	1		
Paraphasia		2		1		
Hematoma Auris			1	3		

Such fleeting delusions would not help us in diagnosis, especially in the scattered visits of private practice, nor would they affect the conduct or attitude of a patient; so that it seems quite practical to neglect them in classification and to place such cases in the simple or depressed class according as

simple mental loss or melancholic delusions dominate the clinical picture. The actual number of cases in which the delusion of grandeur was absent throughout was 66; that is 44 per cent. of the whole series.

On the other hand, the occurrence of these transient delusions and still more the existence of an absurd childish happiness (euphoria) in many cases of the simple form, are much against the old *dualistic* theory of Baillarger, to which Regis and others still adhere. Between the simplest demented case, moping about the ward like an infant, and the "galloping" one wildly struggling and stammering forth tremendous ideas of his strength, wealth and greatness, there is every gradation in our series: to seriously contemplate a distinction between paralytic insanity, and paralytic dementia—that is a fundamental distinction—seems useless, to say the least.

If there be truth in our intimation that the alleged increase of paresis is apparent rather than real, what then was the disposition, nosologically, made of these simple cases which formerly were counted out of the pale of general paralysis—an invidious question perhaps, but one to be faced in the interest of correct diagnosis and prognosis. Charles K. Mills believes that Mendel, for instance, includes in the demented form of paresis many cases which in most institutions are classed as chronic dementias without other qualification.

From Blockley experience, I should say, that the forms of insanity most often confused with paresis of the simple form, are (1) the so-called organic dementias, chiefly those due to hemorrhage, thrombosis, embolism, etc.; (2) pre-senility; (3) dementia praecox; (4) even epilepsy and (5) alcoholic insanity.

(1) The episodes (apoplectiform and epileptiform attacks, etc.) of paresis are waterfalls in the downward current of the malady, leaving a patient weaker in body and duller in mind; and so, when an apoplectiform attack with transient hemiplegia or monoplegia happens to be the first urgent sign

of the disease, it is not strange that the subsequent mental and physical decline is sometimes attributed to true apoplexy, etc. A number of our paretic patients came to us with the diagnosis of apoplexy, of brain tumor, of gross syphilis of the brain.

(2) Hoche in his paper on the early diagnosis of paresis says: "In a case of dementia coming on in the late fifties, it is not of much moment to decide whether it be late paresis or early senility"—a position disappointing in a scientific German, for though senility and paresis be similar in their pathology and though they be almost equally hopeless, yet there are peculiar traits in each which make a diagnosis important for its management; and moreover, the diagnosis can be made nearly always by the ordinary rules to be discussed below.

(3) Dementia praecox, (primary dementia) is common up to the age of 30, and occurs, according to Kraepelin, even in the fifties. Its dominant feature is, like that of paresis, dementia. In dementia praecox the pupils may be unequal; delusions may be present or not; and, when present, they may be as absurd, extravagant, changeful and "polymorphous" as those of paresis. Moreover, convulsions may occur. I have known even Charles K. Mills to postpone the diagnosis of a patient in this very dilemma:

(4) Epilepsy beginning in adult life and due to syphilis or alcohol, or beginning after middle life and referable to vascular changes in the brain—these are somewhat rare; and it is well not to make a diagnosis of epilepsy from convulsions occurring after 30, until every care has been taken to exclude paresis. Moreover, in case No. 125 of my series, we perceive the possibility of paresis supervening upon true epilepsy; this woman has had convulsions about once a month since her 14th year; she is now 43 years of age, and paresis was first suspected by Dr. Lovelace 13 months ago. The character of the patient's convulsions has changed somewhat in the past year; they are more prolonged, less

severe, and are followed by stupor lasting many hours.

(5) In table No. I, it will be seen that alcoholism is predicated of 65 patients, more often of the simple form; and by "alcoholism" we mean prolonged, habitual overindulgence, not the lately-commenced drinking which is often a symptom of early paresis, arising from the "change of character"—the instability, of the first stage. Two of the women had been morphine-habitues for years; one man was an absinthe drinker.

This record is interesting because authorities are generally agreed at the present day that (in the language of Hougberg—"the etiology of general hol, overwork, etc., being subsidiary." But even in a "subsidiary" role, alcohol demands consideration. The whole question of the relation of alcohol to insanity is in an unsettled state. In the German text-books, particularly we discern a tendency to dwell less upon alcoholic insanity as a mental form *sui generis* but to distribute the alcoholic cases among the other classes; thus alcoholic melancholia, alcoholic paranoia, &c., are recognized—not because alcohol is the *essential* cause of the melancholia or of the paranoia, but because it is (1) apparently the exciting cause in these cases and (2) gives a characteristic coloring to them; and by similar reasoning we may speak of an alcoholic paresis. Consider for instance case No. 100 of our series, a man of 35, a hard drinker for many years, who 3 months before admission stopped work partly on account of tremors of legs and hands, partly through jealousy of his wife whom he thereafter followed about the house to watch. He heard voices reviling him and was in terror of being killed.

According to established rules of psychiatry, this patient would have been called a typical alcoholic delusional, had not the diagnosis been cleared up by physical signs including epileptiform convulsions, in one of which he finally died. We confess

that frightful hallucinations do occur in paretics who are not alcoholic, as in case No. 53, a young colored man,* who would yell with terror at the imagined sight of a great dog, or sometimes of a snake, with its jaws open wide to swallow him; but the paretic hallucinations are ordinarily of a pleasant or indifferent character, which may account for their rarity in the statistics of some authors. In table No. I, it will be seen that hallucinations both of sight and of hearing were fairly common in our cases. We confess too that in case No. 100 mentioned above, there was a probable history of syphilis; and we do not say that paresis in this case was due to alcohol and not to syphilis. What we wish to contend is, that *exciting* causes cannot be ignored in relation to paresis, and that among them alcohol is the chief. I notice that in the section of Mental and Nervous Diseases of the American Medical Association this year, Mayer, of Pittsburg, called attention to the inadequacy of the evidence at present for declaring unreservedly that syphilis is the sufficient cause of paresis.

D. E. Hughes is fond of contrasting the great frequency of syphilis in the human race generally—greater than any statistics can demonstrate—with the rarity of paresis; and while such reasoning might easily carry us too far, still it must give us pause in our too hasty acceptance of syphilis as the *sine qua non* of paresis; for if only one in 20 or 30 syphilitics become paretic, there must be some special reason why this one is singled out by the disease. I do not offer in this paper any statistics regarding syphilis, because our records upon this point are very unsatisfactory. The percentage would not be so low as that given by Eickholt (11.8%); but our patients generally deny syphilis, and the various evidences of it, while always studied, were not recorded with the fulness which would make them authoritative.

*There were twelve colored paretics (11 men—1 woman) in our entire series.

The type of case which, for convenience, I have called above alcoholic paresis, has its converse in a case which I treated for delirium tremens in 1897 at the Philadelphia Hospital. On admission to the alcoholic ward, in the evening, he had great tremor, hallucinations of hearing and of sight, and showed the ordinary restlessness, sleeplessness and loss of appetite of the victim of acute alcoholism; but in addition he showed inequality of pupils, and was vehement in declaring himself a prince, owner of scores of horses, &c. The patient had a night's sleep under a hypnotic, and next morning D. E. Hughes went with me to the ward to see my supposed paretic, when to our astonishment, his pupils were equal, and his riches had taken wings. The patient was discharged cured of delirium tremens a few days after, and I have not heard of him since. Regis' idea that belladonna instilled into the eyes at an early stage of paresis may bring out a latent inequality of pupils, made us ponder the question whether alcohol can, in like manner, bring out mental signs in a *potential* paretic or in an incipient paresis.

This case is the only one in which we have had to contemplate the diagnosis of pseudo-paresis upon which the French dwell so much. In our experience the type of alcoholic insanity, as of lead insanity, which may be said superficially to resemble paresis, has been *confusional*;* and the crucial tests of paresis have, we think, been sufficient to enable us to decide.

What then shall we regard as the "crucial tests" of true paresis?

By general consent, the most important is *the state of the pupils*; and speaking broadly, for the sake of impressing the fact, we may say that any abnormality of the pupils, not accounted for by a local lesion, may serve as a sign of paresis. In table No. II, A:

*See also Dercum on Classification of Insanity, Journ. Nerv. and Ment. Dis., Sept., 1901.

TABLE No. II.

A. Pupils in entire series.	B. Pupils in series of 41 casts.
Widely dilated in 9%	Large 5% Wide 12½% } 17½%
Narrowly contracted in 9%	Small 12½% Pin-point 5% } 17½%
Unequal in { R. larger in 32% } 69% { L. " " 37% }	40% 30% } 70%
Reactions apparently normal . . . in 49%	10%
No reaction to light or accom. . . . in 7%	(One side only) 12½%
Reaction sluggish to both L. & Acc. in 24%	17%
Light reaction sluggish } Accom. normal' } in 17%	(One side only) } 15% in 2½% }
Argyll-Robertson in 12%	(One side only) } 5% in 2½% }
Light reac. nil; accom. sluggish in . . .	(One side only) } 17½% in 7½% }
Light Reac. slight; accomf. 'fair'	(One side only) } 17½% in 2½% }
Consensual reac. absent in one eye } when light reac. present }	10%
Consensual reac. slight in both } eyes with light reflex good }	2½%

Argyll-Robertson 5% Proportion.

it appears that inequality is the most frequent change in the state of the pupils and doubtless this is the sign which the practising physician finds ordinarily most serviceable; for though inequality of pupils may occur in a great variety of affections, by

far the commonest cause of it is paresis. On the other hand, abnormalities in the pupillary reactions are found to be the most frequent change when a very refined technique is employed in the examination of the eye. Table No. II, B. represents 41 cases (23 men and 18 women) in various stages of paresis, examined by my colleague, Dr. Elizabeth Lovelace and myself, especially to determine the frequency, in our Blockley cases, of reflex pupillary signs. One interesting fact revealed in this table (II, B) is, that while the pure Argyll-Robertson pupil is rather rare in paresis, the Argyll-Robertson *proportion*; namely, a more marked impairment of the light reflex than of the accommodative reaction—in other words, an Argyll-Robertson *type* of pupil—is almost the rule, since it occurred in 55% of our cases. Irregularity in outline of pupils, excentric position (most often *up* and *in*), springing mydriasis &c., are less frequent and less constant signs. It may be useful to mention what Hoche emphasizes, that reflex pupillary disturbances occurring in *one* eye have as great a value in diagnosis as the same condition occurring bilaterally.

As to the consensual reflex upon which, as an early sign of paresis, Berkley lays so much stress—we paid special attention to it in our series of 41 cases and found it to be an independent sign in a small percentage of cases; though this percentage would be nearly neutralized had we recorded several instances in which the consensual- appeared more active than the light-reflex.

Consisting as it does, in a momentary reinforcement of the light tonus of one iris on exposure of the other eye to light, the consensual-reflex doubtless follows the path of the light-reflex and, *a priori*, it would seem astonishing that its mechanism should be *selected* by degenerative lesions in any considerable number of cases. Moreover, it cannot often happen that being abolished early in paresis, it

should return later;* so that, since in general the consensual-reflex corresponds closely to the light-reflex, we cannot agree with Berkley that the former possesses any decided advantage over the latter as a sign of paresis at any stage. I learn from Dr. G. E. de Schweinitz that this is the conclusion of Swanzy, of Dublin, regarding the consensual-reflex.

It may be noticed in table No. II, B, that the pinpoint pupil and the Argyll-Robertson pupil occurred in equal numbers of cases. Perhaps it is worth mentioning that these two signs, however, do not necessarily coincide. In fact, the "Argyll-Robertson type" of pupillary reaction in our series coincided rather more frequently with mydriasis than with myosis; and in patients with unequal pupils it was the wide one that showed impairment of reflexes more often than the narrow one.

It is a pretty well established law, that an abnormal knee-jerk accompanying any psychosis or neurosis in middle life suggests paresis. Our record of absent knee-jerks (31%) in table No. III, seems high, and

TABLE No. III.

Knee-jerks in entire series.

Increased in	40%	
Diminished in	10%	} 41%
Absent in	31%	
Normal	10%	

it may be questioned whether the Jendrassik method was always properly applied by us; but on the whole this table agrees with accepted teaching, particularly as to the greater frequency of *increase* of the knee-jerks. In three per cent. of the cases we found marked *inequality* of the knee-jerks, which has the same diagnostic importance as any other abnormality of this reflex. In five cases paresis super-

*Although Dr. Wm. G. Spiller tells me that it is conceivable.

vened upon a distinct *tabes dorsalis*; in other words, the so-called ascending type of paresis occurred in 3.33% of our series.

In the every day life of the insane wards there is no more striking event than the "paralytic attack" of the parietic. That a strong man showing hitherto perhaps only slight or equivocal signs of paresis should suddenly be stricken with what resembles epilepsy or apoplexy, is always disconcerting and alarming; but to the diagnostician it is often a casting of the die. From long association with so practical a clinician as D. E. Hughes I know that, to him, no manifestation of paresis has so great *confirmatory* value; and in the light of modern teaching regarding even the tubercle bacillus in lung diseases and tubercasts in diseases of the kidneys, we may say that the paralytic attack of paresis is one of the most *significant* things in the whole range of medical practice—telling us finally that our patient has been drafted to "that war in which there is no discharge".

TABLE No. IV.
Episodes in 149 cases of Paresis.

	Classic.		Demented.		Depressed.	
	Men	Women	Men	Women	Men	Women
Epileptiform	14	5	20	4	5	4.
Apoplect.	8	8	12	2	2	3.
Maniacal.	10	4	8	4	1	3
Stuporous.	5	8	2	5	0	4.
Petit Mal.	4	2	2	3	2	1

Table No. IV shows what is commonly taught: that the epileptiform attack is commoner than the apoplectiform; and table No. V confirms the teaching that the former is also more fatal. That the "maniacal outbreak" is a true "episode" of paresis—in the same category with the epileptiform, and

TABLE No. V.

Causes of death in 52 cases of Paresis.

	Demented.		Classic.		Depressed.	
	Men	Women	Men	Women	Men	Women
Epilept. Episode	6	2	9	2	1	0
Apoplect. „	2	1	1	1	1	1
Staporous Attack	2	1	0	0	0	1
Gangrene of lung, from Epil. Conv.			1			
Empyema	1	0	1	0	0	0
Phthisis Pul.	1	0	1	0	0	0
Pneumothorax	0	0	0	0	1	0
Pneumonia	1	2	1	0	2	0
Dysentery	0	2	0	2	0	0
Pachymeningitis Hem. .	0	0	1	0	0	0
Meningitis	0	0	0	1	0	0
Nephritis	0	0	1	1	0	0
Intern. Hydroceph. . . .	1	0	0	0	0	0

apoplectiform attacks—has long been orthodox teaching. That there is a homology in these various episodes, is shown by the fact that all may occur in succession in one "crisis," epileptiform convulsions ushering in the apoplectiform state from which the patient emerges paralyzed in one-half of the body or in one member or set of muscles—the paretic hemiplegic or monoplegic attacks—while before or after these troubles he is maniacal, and through them all, commonly, he has a temperature elevation of from 1° to 6° or even more. And anyone of these epilept, apoplect, hemipleg. attack, maniacal outbreak, or *temperature-rise* may occur singly in the same patient at another time.

The matter of temperature in paresis is a mooted question. That there is any regular periodicity of temperature rise is held now by almost no

one; paresis is not a febrile disease. But that an isolated temperature rise often represents an *abortive* episode is quite certain.

F. X. Dercum, in his lectures at the Jefferson College last winter, expressed the opinion that the apoplectiform attacks are commoner early in the course of paresis, the epileptiform prevailing later; and our records support this teaching to some extent. What is most striking in this regard is, however, that one form of episode tends to recur in any particular patient and so to characterize the case; thus case No. 42, of the demented type, had epileptiform episodes at frequent intervals in a period of several years; case No. 44 had occasional stuporous attacks resembling uremic stupor but with very little twitching of face muscles; case N. 82 never had any but wild maniacal outbreaks. But when we consider the "minor" episodes (which are much commoner than is indicated in table No. IV—"petit mal") we find that they are decidedly more frequent in the earlier part of the course and that while they may be followed later by apoplectiform seizures they tend to give place later to the "grand" attacks—the epileptiform convulsions. The analogy of this to the evolution of true epilepsy is striking, and it is not the only aspect in which a resemblance may be seen; for the "maniacal outbreaks" of paresis, seldom resembling true mania, are usually quite like the epileptic dream-state, or the twilight-state, as the Germans call the ordinary epileptic insanity.

The convulsion, itself, of paresis is often of "Jacksonian" type and is prone to occur in series with coma, resembling status epilepticus; and ordinarily the convulsion of paresis lasts longer than that of epilepsy, though there is no absolute truth in this. Probably it is wisest to confess, as Ballet does, that the *epileptiform episode of paresis may be entirely identical with essential epilepsy*.

The transient aphasia and paraphasia of paresis

(table No. I) are in most cases connected with the minor attacks.

In order of *scientific* value for diagnosis, after pupillary disturbances, abnormalities of knee-jerks and paralytic attacks, come (1) tremors of face, lips and tongue, with resultant hesitation of speech and tremulousness of the voice, which lacks its normal fullness of tone—its *timbre*; and (2) impairment of consciousness and of judgment.

This impairment of consciousness and of judgment tinges the conduct of the earliest stage of the disease, being taken account of unconsciously by the experienced clinician; and, with the paretic speech disturbance, it composes the *paretic manner* of speech and action, which, after all, establishes the diagnosis in more cases than all other signs of paresis combined. In hospital association with clinicians like Mills, Dercum, Lloyd, and D. E. Hughes I have been impressed with the importance which, whether they would confess it or not, they really attach to this which I have called the paretic manner; it is the shibboleth of paresis—to be appreciated only through experience.

The contributory symptoms of paresis are numerous and it is perhaps true that none of them is characteristic. Thus "wandering from home", mentioned in table No. I, is a trait of the adolescent, of the senile, of the epileptic, of the confusional; but the first leaves home in a restless, persecutory mood—his "orientation" being preserved; the senile is easily recognized and his perambulations are habitual; the epileptic alone may give us great difficulty in the absence of a history. The wandering of the paretic seems to be the manifestation of a *confusional* attack in which there is a dominant impulse to ramble. It is the true "*mania errabunda*" of the older writers. In Blockley we have learned to suspect paresis whenever an adult patient is brought to us with this history of aimless, excuseless wandering from home.

The hypochondriacal delusions of paresis have considerable significance. They seem to be gradually evolved in the very earliest period of the disease, giving character to the next or "hypochondriacal stage"; and they are said thereafter to be prominent in the depressed form of paresis. In table No. 1 it will be seen that our patients betrayed hypochondriacal delusions. In each of the three forms of paresis, I may add, it was found at all stages. The delusion of pregnancy (table No. 1) a curiously common symptom in women, to which I have seen no reference in the literature, might be included under hypochondriasis. As Ballet first pointed out, it is one of the principal dilemmas in the diagnosis of paresis, to distinguish this disease at an early stage (the neurasthenoid stage of Dercum) from true neurasthenia; it appears sometimes to be impossible. Often the hypochondriacal delusion has the character of an obsession—in case No. 80 of our series, there was true *folie du doute*—so that some paretics are constitutional neurasthenics, in the sense of Morselli, and degenerates, according to Magnan's view of the obsessions.

In the forthcoming second volume of his work on Neurology, Charles K. Mills will declare his belief that paresis is due to syphilis on a neuropathic basis. This may be regarded as the very latest teaching upon the etiology of paresis; but it is more comprehensive than at first sight appears, as the history of this question shows.

Esmarch and Jessen first (1857) advanced the theory that paresis is due to syphilis (Hougborg); but not until 1878, when the great name of Fournier became associated with it did the theory attract much attention, and then a current of opinion, mainly German, set in towards the unitarian view championed by the great syphilographer. Regis, a partial convert, in 1888, proposed a compromise doctrine; that paresis is due to syphilis acting with a *hereditary disposition*; that is, syphilis in the hereditary degenerate. But since the conception of degeneration

has undergone a metamorphosis at the hands of some very able members of the French school—who show that a like vulnerability of the nervous system may be acquired—the term *neuropathic* seems to be safer, as embracing both inherited and acquired sus-

TABLE No. VI.
Family histories in 89 cases of Paresis.

	Father	Mother	Brother	Sister
Insanity	8	6	2	1
Suicide	1	1		0
Imbecility	1	0	1	0
Paresis	1	2	1	0
Epilepsy	0	1	0	1
Hysteria	0	0	0	1
Locomotor Ataxia	1	0	0	0
Cerebral Palsy	0	0	1	0
"Stroke"	7	8	0	1
Alcoholic	10	0	1	0
Chorea	0	0	1	0
Consumption	10	12	2	6
Cancer	2	3	0	0
Heart Disease	2	5	0	0
Asthma	2	1	0	0
Bright's	3	1	0	0
"Dropsy"	1	2	1	0
Rheumatism, Chr.	0	1	0	0
Diabetes	0	1	0	0
Blind	0	0	0	2
Sun Stroke	1	0	0	0
Syphilis, Malignant	1	0	0	0
Lead Poisoning	1	0	0	0
Head Injury	1	0	0	0

ceptibility to nervous and mental disease. It is thus that Dr. Mills' statement in one way may be made to reconcile the older view that paresis is due to alcohol, overwork, &c., and the modern one that syphilis is essential.

That purely hereditary degeneration is a strong factor in the etiology of paresis, is shown in table No. 4, a summary of which reveals a percentage (75%) of vicious constitutional disease as high as that found in our Blockley statistics of dementia praecox, the several forms of which are recognized as peculiarly degenerative.

Grainger Stewart, it appears, was the first to conceive the idea that paretics free from this neurotic taint have greater chance of *remission*. It seems worth while to inquire into this, for remissions have considerable importance in prognosis. The mental excitement of the paretic is often in abeyance for weeks amid the quieting influences of the hospital, and may lead the friends to speak of the patient as "recovered"; though the clinician realizes that merely the foam has cleared from the surface—that (in terms of the dualistic doctrine) his patient is still a paretic dement, his paralytic insanity alone having undergone remission.

All authorities, however, recognize a true, well-nigh complete remission simulating recovery, and this constitutes one of the great problems connected with paresis; for to know how this Tantalus' Cup is held to our patient's lips for months—even years—(though it be always snatched from him at last) would be to know the secret of his disease and perhaps the cure.

Remissions occurred in the following cases of our series:

Case Number.	Duration of Remission.	Family History.
46	Two years	Neg.
80	Seven months	"
85	One year	Mother "stroke"
		Brother Chorea.
95	11 months	Pat. grandfather "stroke"
99	9 months	Neg.

The family history of these five patients, given in the right-hand column, contains no instance of the graver degenerative diseases; indeed some authors would not regard apoplexy as imposing any hereditary stigma whatever. At any rate the percentage of "vicious constitutional disease" in these five cases is much under that of the general record in table No. VI, and so may be said to support Grainger Stewart's view.

In case No. 95, the first signs of paresis were noticed a day or two after a collision between an automobile and the bicycle on which our patient was riding. He was treated in a hospital for bruises and shock. The latter induced a confusional state, in the midst of which tremor of the lips attracted attention, and shortly afterwards, inequality of the pupils. On admission to Blockley he presented the picture of classic paresis. There are other instances in our series (table No. 1) of this which some authors call traumatic paresis. In at least two other cases paresis *appeared* to originate in profound mental ("moral") shock. At most we may only admit these as "exciting" causes; but that trauma did play this role in Case No. 95 seems probable from the fact that the long remission was established only a few weeks after the accident.

If we look upon remission as a *tendency towards recovery*—a temporary triumph of the reparative processes—it is perhaps reasonable to suppose that *some element of the cause* of paresis is in abeyance in cases which have remissions, and, finding the

neuropathic taint slighter, in such cases, we may logically conclude that neuropathv is a common etiological element of the disease. Thus remission may be regarded as a considerable argument in favor of the view held by Dr. Mills.

It may be profitable to suggest two lessons from our study of paresis. First, for our patient : That immunity from paresis rests not on freedom from the great infection alone, but, as the older writers believed, on abstinence from *all* excesses. Second, for ourselves : That diagnosis, the principal thing required of us in the present state of our knowledge of paresis, depends so much upon a practical acquaintance with the "paretic manner," that no amount of fine training in the best schools can take its place. Impressed with this fact by daily contact during several years, with some scores of the best graduates of our Philadelphia medical colleges, I would urge the importance of *teaching in the asylums*. An hour in the wards is of more value than many lectures.

NOTES FROM THE PATHOLOGIC LABORATORY OF THE JEFFERSON MEDICAL COLLEGE.

BY

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ADRENALS CONTAINING PIGMENT CELLS RESEMBLING THOSE OF THE LIVER.*

Right Adrenal.—The gland measures 6 cm. in its longest diameter and 3 cm. in its greatest width. It is 1.5 cm. in thickness. Upon section of the specimen, which cuts with ease, the cut surface is of a uniform dark yellow color, firm in consistency with no demonstrable areas of necrosis.

Upon histologic examination, after staining by various methods, the mass is seen to be made up of adrenal structure, arranged very irregularly in small and large lobules. The cortical portion of the gland is for the most part normal in distribution. In one or two small areas there is an absence of the zones and in their place is an accumulation in masses of closely packed cells that resemble those of the normal gland. The medullary portion of the organ is very irregularly mapped out.

The lobules above mentioned are limited by masses of connective tissue in which few lymphoid cells and polymorphonuclear leukocytes are seen. In some of the lobules there is the appearance of a cortical portion, *i. e.*, the acini in rows or zones. In most of the lobules, however, there is an irregular arrangement of the contained acini. The bloodvessels throughout are engorged; small and large accumulations of red blood cells are seen scattered throughout the organ, but most marked at the periphery.

The capsule is slightly thickened and in the connective tissue, entirely outside of the gland structure, are seen small masses of cells that resemble acini of the gland proper, separated by delicate processes of connective tissue. The sections cut from the gland are more or less triangular in outline and

* I am indebted to Dr. Joseph Saller for the specimens.

near the apex of this triangle is a small area, 5 mm. in diameter, that in the unstained condition is much darker than the surrounding structure.

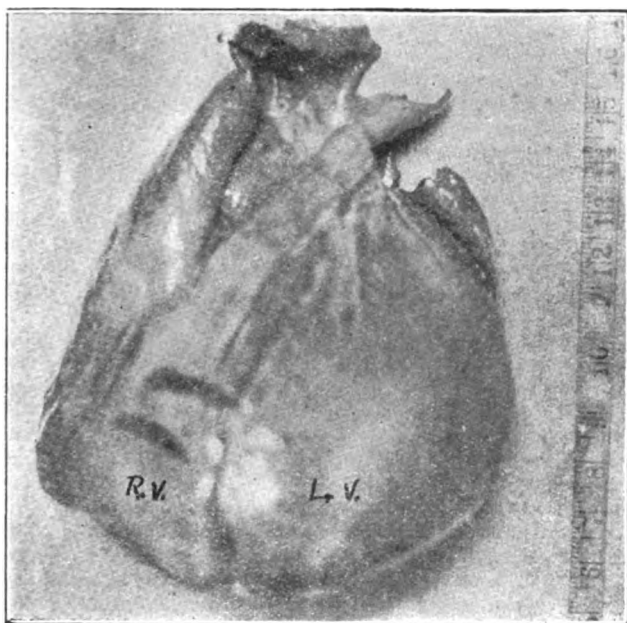
Histologically, this area is made up of large, irregularly polygonal cells, arranged in cords, containing one and sometimes two or even three large round nuclei. The protoplasm is granular and dark and small fat globules are also present. They give a positive reaction to the test for glycogen, while the remainder of the specimen does not. The area in some portions is separated from the adrenal structure by fibrous connective tissue, but at other points is seen to merge gradually into the adrenal. Where this latter condition is noticed, an occasional solitary cell, or groups of two or three cells, can be seen as far up as the cortical portion. Another interesting feature is the presence of a number of lymph follicles scattered throughout the specimen, but most marked in the central part.

Left Adrenal.—The organ measures 5 cm. in its longest and 2 cm. in its shortest diameter, and is 0.5 cm. in thickness. Upon section, the cut surface is yellowish in color and presents a small, sharply outlined nodule, 5 mm. in diameter, of a slightly paler color than the remainder of the organ. No areas of necrosis or caseation are observed.

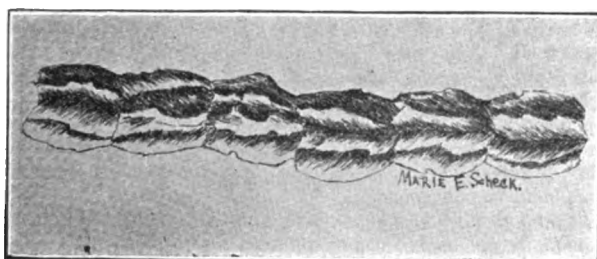
Histologic Examination.—The cortical portion of the gland is for the most part regular as regards the zones. The medullary portion is faintly marked and in some areas is not demonstrable at all. There is an irregular arrangement of the acini of the gland where the medulla should be.

In one or two areas there are seen masses of cells, irregular in shape, staining more darkly than the cells of the organ and separated or limited by small bands of connective tissue. These irregular cells extend in quite a lawless manner in the areas mentioned, suggesting carcinoma, though no malignant process in other organs is present. Beside the cells mentioned above, there are columns or rows of large polygonal cells, markedly granular and pigmented, containing one and sometimes more than one nucleus. Some of the nuclei are oval, others round, and a few are coarsely granular. Some of these cells are 20 microns to 30 microns in diameter, while some of the nuclei are 10 microns in diameter. These rows of cells are seen distributed throughout the different regions of the organ, in the cortical and in the medullary portions. They give a positive reaction to the test for glycogen, while the cells of the adrenal do not. Small areas of hemorrhage are seen in the organ, while irregular areas of lymphoid accumulations are present, especially in the cortical portion.

Rolliston¹ mentions that the cells of the adrenal in children are not pigmented, while in adults pigment is present. In



Heart with bifid apex.



Teratological form of the Tænia Saginata (natural size).

negroes the cells of the cortex are said to be extensively pigmented.

Stillling claims that the cells of the medulla are chromophilic.

Orth refers to a green coloration of the medulla on adding a solution of perchlorid of iron, as a sign of chromogen in the cells of the medulla.

When fresh, the cells of the medulla stain brown with bichromate of potassium; blue with persulfate of iron. The blood spaces are surrounded by the cells so that there is some resemblance to the arrangement in the liver, of cells and capillaries.

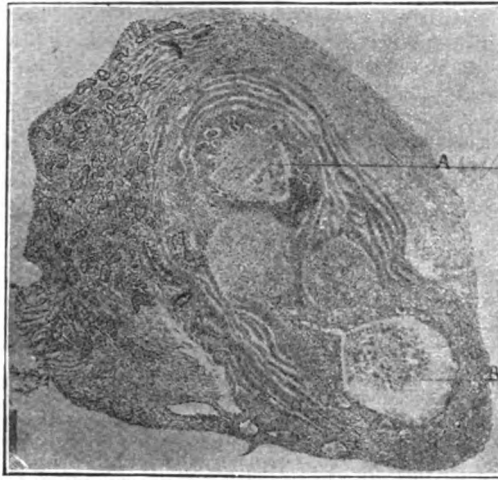
Eurich² reports the occurrence of a mass which occupied the position of the right adrenal, but was separated by two inches from the corresponding kidney (which was displaced downward). The space between the kidney and adrenal was occupied by a tumor almost spheric in outline, of a purplish hue and encapsulated. Upon its upper pole was perched the adrenal, which was in nowise involved by the tumor mass, and from which it was separated by the capsule mentioned.

Microscopic examination revealed glandular-looking cells, without cell wall, irregular in shape, the polygonal form prevailing and containing an oval nucleus centrally situated and varying considerably in size. If bichromate specimens are examined, most of the cells appear to contain a diffuse, yellowish-brown pigment. In these preparations also there is a hyalin-looking, transparent substance found in veins and their branches, but apparently not in the larger vessels. It stains yellowish-brown with picrocarmin, pale-red with lithium carmin, faintly with alum carmin, and not at all with hematoxylin. The arrangement of cells is very irregular, and is determined by an intricate network of capillaries, veins, sinuses and blood channels, between which the cells are placed. No traces of fat or glycogen could be detected in the cells by the usual methods. (No diagnosis is given as to the nature of the tumor, but the supposition is that it probably represents a hyperplastic condition of the adrenal.)

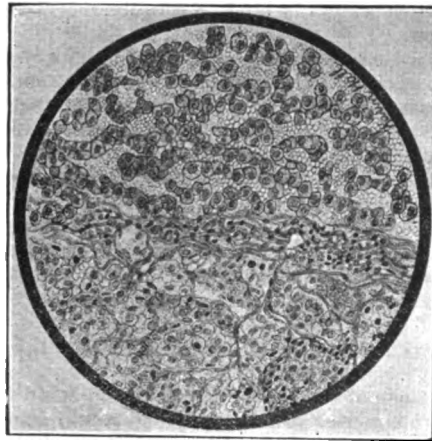
Schmorl,³ in two cases of accessory adrenal, found in one that the cells of the zona fasciculata showed fat globules and yellow pigment, and in the other simply mentions that the cell protoplasm was pigmented.

Chian⁴ mentions in a case of ectopia of the adrenal that just external to the centrum, pigment cells were noted. Another case by the same observer occurred in the broad ligament of a woman. In this case the pigment zone was well marked and the centrum especially so.

Dagonet⁵ mentions, in discussing ectopia of the adrenal,



Appendix with two lumina—A and B the lumina.



The lower half of specimen shows adrenal tissue, while the upper half contains the liver-like cells.

that in children the centrum was red and the vessels filled with blood, while in the adult the centrum was usually pigmented and dark.

AN APPENDIX VERMIFORMIS WITH A DOUBLE LUMEN.*

The appendix was obtained from an adult male, aged 56, who died from inanition, resulting from carcinoma of the pylorus.

The organ measures 5 cm. in length and 1 cm. in diameter, and is firm and fibroid. The lumen is so much obliterated that only a pin point can be passed into it. Upon histologic examination the organ shows the result of a chronic catarrhal process. The most interesting point is the presence of two lumina, which can also be seen with the naked eye. Each lumen has its set of simple tubular glands, solitary follicles and muscularis mucosæ. Beside this feature there are present irregular groups of epithelial cells in small alveoli, suggesting secondary involvement of this organ by the growth in the stomach.

AN ADULT HEART WITH BIFID APEX.

The heart presented is from an adult male, aged 24, who died of enteric fever in Jefferson Hospital, service of Dr. Hare. Weight of organ, 180 grams.

The interesting point about the specimen is the condition of the apex, which is slightly bifid. Naturally, this is a congenital malformation.

There is a distinct groove separating the apex of the organ. This groove upon the anterior surface measures 2 cm. in length, upon the posterior surface 1 cm., and its greatest depth is 1 cm.

The anastomosis of the coronary arteries can be very plainly seen at the apex, as, according to Dr. Samuel West,⁶ there is a very free and complete anastomosis between the two vessels. The accompanying photograph illustrates the condition very well. One view shows the anterior surface of the organ, while the other shows the heart tilted up and looking directly at the apex. (The light areas seen in the picture are "halation" spots produced by the glistening surface of the organ.)

A PECULIAR TERATOLOGIC FORM OF *TENIA SAGINATA*.

This specimen of worm here presented is interesting from the fact that upon cross section it is star-shaped. In none of the authorities consulted could a reference to such a monstrosity be found. Alluding to this specimen, Dr. John R. Mohler, of the

* I am indebted to Drs. Wallace and Neuber for the specimen.

- Bureau of Animal Industry, in Washington, D. C., writes that the specimen is unique. He has seen "three-sided segments and various other freaks in this worm, but this is the first star-shaped variety. Some branched off from the side like yeast-plants, and still others had the three-sided segment, while one was covered with protozoa."

This specimen has probably six to eight suckers on the head, making it more difficult to dislodge. I am indebted for the parasite to Dr. Bradeen, of Colorado, who at a late date wrote that the head had not yet been passed.

REFERENCES.

- 1 British Medical Journal, 1896.
- 2 Journal of Pathology and Bacteriology, 1900, Vol III, p 502.
- 3 Ziegler's Beiträge, Vol IX, 1891.
- 4 Zeit. für Heil., Vol. V, 1884.
- 5 Zeit. für Heil., 1885.
- 6 Lancet, June 2, 1883, p. 945.

MICROCHEMICAL REACTIONS OF TUBE CASTS*

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Having recently been interested in the microchemic reactions of certain necrotic productions, it occurred to me to study tube casts by some recent methods. It is not my purpose at the present time to take up the chemistry of renal casts, only to call your attention to certain reactions microchemic in character and directed toward a determination of the chemistry of these bodies. Various views have been held as to the origin and composition of renal casts.

Rovida¹ investigated the origin of these bodies, and looks upon them as secretion products arising from the epithelial cells; this view is adopted by Key²; Bayer³ recognizes their origin from the epithelial cells of the tubules but looks upon them not as secretion products but the results of destructive metamorphosis. Mayer's⁴ conclusions antedating the work of Rovida, are practically identical with those of the last named writer.

Langhans⁵ adopted both suggestions, believing that certain casts resulted from changes in the

*Read before the Philadelphia Pathological Society, Feb. 13, 1902.

**From the Laboratories of the Jefferson Medical College Hospital.

1. Cited by v. Jaksch.

2. Schmidt's Jahrbuch, CXIV, 1867, p. 171.

3. Arch. d. Heilkunde, 1868, p. 136.

4. Virchow's Arch., V. 199, 1863.

5. Virchow's Arch. LXXVI, 1879, p. 108.

epithelial cells and that others were true secretion products. Knoll⁶ concluded that chemically, and probably structurally, tube casts were composed of elements whose nature did not correspond with other known urinary constituents. Traube, Rindfleisch, Klebs, Bartels⁷ and others have taught that the cylinders were really solidified exudates and Burkart⁸ would have us believe that tube casts are invariably essentially of inflammatory origin. Posner⁹, Torok and Pollak,¹⁰ Neubauer and Vogel in common with a number of authorities believe that they are altered albumin that, under the influence of the urine, has solidified in the tubules, and Ribbert¹¹ came to the conclusion from experimental studies that hyalin casts might result from transformation of albuminous exudates. The repeated suggestion that they are fibrin more or less modified has generally met with disfavor.

Of recent years I am not aware that anything of importance has been added to our knowledge of the origin, structure and chemistry of these bodies; it has not been my good fortune to add anything startling, but the following experiments have been conducted for the purpose of demonstrating something of the micro-chemistry of casts.

Technic:—Urine obtained as fresh as possible, often withing two or three hours after being voided, was rapidly sedimented in the centrifuge, the sediment repeatedly washed with normal salt solution,

6. Zeit. f. Heilkunde, V. 269, 1884.

7. Arch. f. exp. Pathol. u. Pharm., VI, 1877, p. 113.

8. Die Harncylinder, 1874.

9. Virchow's Arch., LXXIX, 1880, p. 320.

10. Arch. f. exp. Pathol. u. Pharm., XXV, 1889.

11. Centralbl. f. d. med. Wissensch., XLX, 305, 1890.

and fixed in the centrifuge tubes by the following methods:*

(1) Increasing alcohol, (2) Zenker, (3) Marchi, (4) Müller. The fixed sediment was then stained by a number of methods, hematoxylin alone and with eosin and also with picric acid; saffranin in various combinations, and by a number of mucin stains among which being that of Paul Mayer¹². This reagent,—muchematein—as originally suggested by Mayer, is probably one of the purest mucin stains that we possess; lately Harris¹³ has corroborated this opinion.

Sudan III and osmic acid have been used for demonstrating fat. The former reagent was applied as follows:—

Casts fixed in non-alcoholic fixation were thoroughly freed from the reagent and treated with a solution of Sudan III in 70 per cent. alcohol, washed in water and mounted in glycerin jelly. Osmic acid yielded much better results, beautiful examples of fat-bearing casts having been obtained by the following technic:—Sediment obtained as already directed is washed in Müller's fluid and transferred to Marchi's fluid, using the regulation formula of 1 part of one per cent. solution of osmic acid and two parts of Müller's fluid. The reaction usually

*There is no difficulty in fixing, washing, staining, dehydrating (when permissible), clearing, etc., directly in the centrifuge. There is astonishingly little fragmentation of the casts. Staining methods that permit of dehydration are followed by alcohol and appropriate clearing agent, out of which the drop for a balsam mount is taken; methods that require glycerin jelly are simpler, but the results are not permanent.

12. *Zeit. f. wiss. Mik.*, XIII, 1896, p. 38, also, *Mitth. Zool. Stat. Neapel*, XII, 2, 1896, p. 303.

13. On the Alterations Produced in the Large Intestines of Dogs by the Amœba Coll. by Heat, and by Various Chemical Substances, etc. Hatfield Prize Essay, Philadelphia College of Physicians, 1901.

reaches its height within four or five days and the casts may be left indefinitely in the fluid.

The muchematein is used according to directions given by Mayer, the watery solution being preferred. It stains more rapidly than hematoxylin and practically all of my specimens appear to be overstained although some of them were subjected but a few moments to the action of the stain.

Results:—All hyaline casts may be divided into two groups. (1) Hyaline casts that stain faintly with the mucin stain. These casts are usually small, smooth and free from cells and fat. (2) Hyaline casts that stain intensely giving the mucin reaction to a degree that renders them almost opaque.

All granular casts in my collection, that are not fatty, give an intense mucin reaction. Sections of such casts show that the mucin reaction is not restricted to the periphery but is present in the matrix.

Epithelial casts commonly give a decided mucin reaction, the intensity of which seems to be directly proportionate to the granularity of the cells,—the more granular the cells the more evident the mucin stain. Casts of this group are not infrequently found in which one end may show a most intense mucin reaction and cells at the other end give the reaction but faintly,—the histologic element (epithelium), staining quite clearly. It would appear the more advanced the degenerative or necrotic change, the more evident the mucin reaction; the mucin reaction commonly quite disappears before the advent of fat, as the two reactions have not been observed in the same cast nor has one been obtained with even the appearance of the second body in another part of the cast.

The origin of the mucin in casts has been considered but it can not be said definitely to be determined. Its presence in the epithelial elements of casts and its apparent increase in those undergoing fragmentation and disintegration would seem to indicate that in some way it, at least in part, is a product of necrosis or degeneration—probably both—arising in the cellular elements cast off from the renal tubules. The possibility of cells imbibing mucin from urine rich in some form of the substance has been considered but does not seem likely. The exact nature of the mucin found in the casts is still undetermined; of the many mucins and pseudomucins known to chemists it is impossible for me to say just which responds to the microchemic tests applied.

Fatty casts are found composed of masses and groups of fat globules possessing slightly different characters depending upon the quantity of fat and the grouping, and held in position by some matrix the exact microchemic nature of which has not been possible to determine.

(1) Some fatty casts are made up almost exclusively of small globular black masses evidently fat, fairly distributed throughout the length of the cast; in such casts no cellular structure can usually be identified. (2) Casts that contain aggregations of fat usually in the shape of variously sized globules, some of them practically amounting to granules, others nearly the size of nuclei or of epithelial cells. (3) In still another group of casts epithelial cells can be seen the protoplasm of which contains fat. In such cells the fat is usually finely distributed through the perinuclear protoplasm, although I

feel quite sure that in some of them it was possible to detect the intra-nuclear presence of fat.

Observers seem to have agreed that fatty casts result from fatty metamorphosis of renal epithelium and to this view the observations here recorded offer no contradiction. It seems equally probable that other casts are also the result of necrosis or degeneration of renal epithelium and that during the progress of the retrograde change mucin becomes a conspicuous constituent. As mucin and fat do not appear to be coincident bodies in the same cast it would seem reasonable to assume that the presence of one or the other is determined by some condition the exact nature of which is not apparent. Both may be present in the same urine but it has not been possible to say why they do not occur strictly together.

THE CAROTID BODY: ANATOMY, HISTOLOGY, EMBRYOLOGY AND TUMORS ARISING FROM IT.*

BY

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HISTOLOGY AND ANATOMY.

The first intimation as to the existence of this organ was in all probability given us by Haller,¹ who, in 1748, wrote of the "*de vera intercostalis origine*," and again, in 1744, of "*de nervorum in arterias imperio*." Newbauer,² in 1772, clearly refers to such a body in his "*descriptio nervorum cardiacorum*." Andersch³ gave us a practical description of the organ in 1751, although his work is recorded in "*tract anatomico-physiologico*," 1797. After that date the body was overlooked by many distinguished anatomists until 1833 when Mayer⁴ recognized that beside two or three cervical ganglions there are other small ganglions in the neck which had been found and described by several authors and which are more or less intimately associated with the sympathetic nervous system. Another ganglion of more importance, and according to his knowledge not previously described, was the structure now called the carotid body which he located in the angle formed by the bifurcation of the carotid. It is the size of a grain of rice, oval in shape, red, firm and vascular. In structure and consistency it resembles the superior cervical ganglion. By means of a small band it is attached to the carotid at the bifurcation. The body is in relation with the "*nervus mollibus*," formed by a plexus from the superior cervical ganglion; a branch from the glossopharyngeal nerve, after sending a branch to the "*nervus mollibus*" penetrates the ganglion; before entering the ganglion, however, it receives another branch from the vagus. In order to find the ganglion one need only remove the common carotid together with about an inch of the internal and external carotids. Mayer found the ganglion

* From the laboratories of the Jefferson Medical College Hospital
Read before the Pathological Society of Philadelphia, April 14, 1904.

in horses and in calves in the bifurcation of the common carotid; in calves the relation between the ganglion and the "*nervus mollibus*" is greater than in the human being. Mayer says the ganglion intercaroticum in its relation, its form and its texture may be likened to the celiac axis.

In the same year Valentine⁵ described the body as pear-shaped, the apex of the pear pointing downward; it is gray in color and of firm consistency, and difficult to free from the surrounding structures. After maceration the internal structure is composed of reddish-white fibers, bands or septums which are interlaced and held together by fibrous tissue. The greater the angle of the carotid bifurcation the more superficial the organ. Maceration in water, continued for several days, dissociates its capsule and makes clear its internal interlacing structure and the ganglionic character of the organ. Valentine believed the carotid ganglion received communicating branches from the vagus. Branches are given off from both sides of the gland, part of which goes to the artery and the other part unites with the "*nervus mollibus*" so the gland is completely encircled with nerves. The band uniting the carotid body to the carotid artery, by microscopic examination, is found to be made up of nerve fibers.

Luschka,⁶ in 1862, gives us the first microscopic description. He says the carotid body is not a ganglion in the ordinary sense of the term, but that it is a gland-like appendage, or part of the sympathetic structure of the neck. It is surrounded by adipose tissue and a sheath from the adventitia of the carotid, which must be cut before the gland becomes visible. It is connected with the common carotid by means of a band of elastic tissue, which becomes lost in the tunica media of the artery. The gland is firm and elastic; if compressed between two glass plates and examined with a lens, it is found to be composed of large and small spaces bordered by thick walls; the external portion of the walls is associated with the fine connective-tissue substance containing many oblong cells. He divides the spaces into two types, one vesicular, the other tubular. The tubules can be traced some distance; their course is usually very irregular and they lie between the vesicles. The vesicles and tubules contain round, granular, clear, and nucleated cells. Occasionally the cells in the vesicles resemble cylindric epithelium. He did not find any cells clearly ciliated, although some resemblance to ciliation could be

detected. The arrangement of the cells in the vesicles and in the tubules is irregular; some, however, simulate the arrangement of the epithelium. The stroma of the organ contains many cells like those in the vesicles, either isolated or grouped. The organ, he says, receives its blood supply from the common carotid by means of a single branch, which divides and subdivides; the branches penetrate the organ and become lost in the stroma. He has never been able to find a capillary network.

Between the internal and the external carotid, Luschka finds a twirl of nerves, which he calls the inter-carotid plexus, and which, he says, is made up of fibers from the superior laryngeal, the glossopharyngeal, and a number of branches from the superior cervical sympathetic ganglion. He believes the purpose of this plexus is to unite the sympathetic and the cerebrospinal nerves. So far as his observations go, the fibers from the superior cervical ganglion to the carotid plexus are related to the carotid gland; they also pass to the external carotid and its branches, as *rami vasomotorii*. In the substance of the carotid gland the nerves break up into a network, which penetrates the vesicles and tubules of the gland. Polar ganglion cells, related to the nerve fibers, are rarely found, but apolar cells, either in groups or isolated, are abundant; at times they are enclosed within the membranes of the vesicles and tubules. Those which Luschka believes are nerve cells always remain posterior to that part he designates the glandular portion of the organ.

J. Arnold¹ in 1865 takes the ground that Luschka's description of the organ is incorrect and that it does not contain gland structure. He says the carotid body is supplied by four vessels derived either from the common or external carotid arteries, upon each of which hangs sometimes an oval and at other times a round lobe composed of three or four lobules depending upon the division of the main artery. The vessels forming the lobules of the glomeruli possess thin, circular muscle layers. The epithelium seen in the average artery has reached a high degree of development. The efferent arteries soon after leaving the glomeruli surround the lobules and in association with the network of corresponding glomeruli form a widely meshed network. In noninjected preparations the apparent tubules are filled with finely granular nucleated cells, in the injected preparations they are occupied by gelatin. Fibers from

the vagus, glossopharyngeal and the sympathetic form a plexus at the division of the common carotid between the branches; many fibers from this plexus penetrate the capsule of the organ. The fibers after reaching the inner portion of the body surround the lobes and lobules in a network. The gland, vesicles and tubules of Luschka are identical with the divisions of Arnold's glomeruli. The occlusion of the tubules with epithelial masses is apparent only. The ganglion cells in proportion to the presence of the nerves are not so abundant. Apolar ganglion cells surrounded by a common capsule in which are also epithelial-like cells are not present.

Switzer⁸ is convinced of the ganglionic character of the carotid body. Sertoli⁹ found a fibrous band surrounding the body described by Luschka but regarded it as formed of bloodvessel. Pfoertner¹⁰ accepts Arnold's view; he recognized the tubules and acini as being formed from bloodvessels, the isolated bodies as glomeruli and says the sizes of the latter vary; sometimes they are composed of few, other times of many vessels. He often observed several vessels merged into the wider one which he held to be a vein. He found many nerves, no ganglion cells but fat in the stroma.

Kölliker¹¹ merely refers to the work of Luschka and Arnold upon the carotid body. Eberth¹² believes the carotid body, like the gland of Luschka is composed of whirls of vessels, which are mainly capillaries, some are normal, others widened. Frey¹³ thinks the tissue of the carotid body is largely vessels; the cells present he likens to the cell element seen in the adrenal or to Waldeyer's plasma cells.

Heppner¹⁴ says this body varies in size from that of a hemp seed to a cucumber seed; it is situated for the most part behind and in the median line of the common carotid, its apex projecting a short distance beyond the bifurcation. The organ is composed of a stroma and gland structure. The peripheral stroma is a continuation of the band connecting it to the carotid artery, in which band are many elastic fibers. From his preparations he is unable to decide whether to regard the lobules as cross sections of vessels, as held by Arnold, or glandular, as maintained by Luschka, since, in peripheral lobules, he can recognize structures in the alveoli that may be regarded as a membrane; he inclines to the latter.

Marchand¹⁵ finds in an embryo of four months, the carotid body composed of a loose connective tissue, in which are many vessels and nerves. In the periphery

the cells and fibers are arranged concentrically. At points the spheric groups of cells (zellballen) break up and gradually merge into a delicate fibrous tissue. In other places the cells form columns which very often show an inner relation to the vessels. Careful examination of the spheric groups of cells reveals lumina bounded by fine lines and filled with red blood cells. In the adult body two elements share in the construction of the lobules, namely, cells and vessels which are closely related to each other. In the connective tissue are collections of cells, the largest of which are sharply circumscribed, at times by a delicate band of fibrous tissue. These groups simulate gland acini, but they possess a fine intercellular reticulum. The collections of cells either embrace the capillaries or are in contact with one side.

Paltauf¹⁶ says the lobules are composed of many vessels that are surrounded by a narrow band of fibrous tissue upon which is situated a stratified layer of oval nuclei. In chrome-osmic hardened preparation he recognized the vesicles, especially those limited with homogeneous walls and in which are the oval nuclei, as bloodvessels. He demonstrated muscle fiber nuclei in their walls. According to his investigations, the carotid body is not composed of whirls of vessels only, but the winding vessels that form the lobules and correspond to the glomeruli are surrounded by a reticulum of delicate fibrous tissue, in the meshes of which are cells, some of these lining the vessel. He is inclined to retain the name *glandula carotica* in the same sense as we speak of lymph-glands and thymus gland.

Kopfstein,¹⁷ in an article on tumors of the carotid body, expresses the conviction that the normal organ is composed of vessels and cells. It presents lobulated structures, and is surrounded by a capsule. The cells are found between the vessels, and simulate in structure an acinus. These cell collections are intimately associated with the vessels. They are either concentrically arranged around the vessels or are closely united to one of their sides. Anatomically the body appears to be connected with the sympathetic system, since nerve fibers from the cervical ganglion enter it.

Princeteau¹⁸ believes that according to researches of Rieffel, it is not an intercarotid but a retrocarotid corpuscle, attached to the carotid by a fibroelastic ligament called the ligament of Mayer. He says its position varies at times, in three cases he found it above the

bifurcation and in one case on the posterior surface of the internal carotid. The arrangement of the blood-vessels has struck Princeteau as being very curious; the arteries supplying the body, break up in small tufts, each of which is made up of five small arteries. The main artery runs from below upward, one branch of which passes downward to reach the inferior pole. In the body the ramifications of the arteries can be followed for some distance. He has found usually four or five nerves that depart from the superior pole, run parallel to one another, and enter the intercarotid space where they intermingle with numerous nerve fibers to form the intercarotid plexus. The nerves are very numerous and emanate from various sources. In some cases he has seen them spring from the intercarotid plexus, but in the greater number of instances they came from the carotid body. Summing up its structure, he concludes that the inferior pole is arterial and ligamentous and the superior pole venous and nervous.

Kohn¹⁹ says that between the two carotids, and above the bifurcation, lies an organ peculiar to itself, which he designates "paraganglion intercaroticum." The cells, the nerve fibers and the ganglion cells are derivatives of the sympathetic system. The specific elements of the organ are the chromaffin cells, which spring from the sympathetic (embryonic) cells. Their cell substance is very well preserved by the chrome salts but with other fixing agents preservation is poor; with the chrome salts they stain yellowish. The ganglion is abundantly traversed with nerve fibers in which lie the spheric groups of cells and the ganglion cells of the intercarotid nerve plexus. The organ is richly vascular but the vessels present nothing peculiar in their arrangement nor in their construction. Kohn says this body is neither glandular, as held by Luschka, nor is it glomerular, as maintained by Arnold; it belongs to a category of its own.

Heinleth²⁰ thinks the carotid body has a lobulated architecture. The structure of the lobules is composed of vessels and cells which bear a close relationship to one another. The lobules have the appearance of vesicular spaces, some of which are round, others tubular, they are either empty or contain granules, they possess limiting walls which at times are thick, containing many nuclei. The large spaces have laminated walls possessing muscle fibers. The small, more loosely built lobules, show between the vesicular spaces many round

apertures lying in a reticulated connective tissue substance in which are round and oval nuclei.

Usually a nucleus lies along the periphery of each aperture, at times one lies in each lumen. The cells of the apertures contain an abundance of granular protoplasm; they are either low columnar or polygonal and simulate epithelial cells. The nuclei are often eccentrically placed. The apertures have no relationship to the reticular structure, except that they lie in contact with it. By injection the cells in the apertures are particularly conspicuous, they appear to line parts of the vessels and parts of the apertures in the reticulated structure. Reclus²⁹ says there is present more than simple vascular glomeruli; between the vascular meshes are cells which have an intimate relation with the vessels. Szymonowicz and MacCallum³⁰ think the carotid body is divided by connective-tissue septums into follicles which are filled with masses of small round cells, the so-called "zellballen." These cells resemble epithelium, they are either round or polyhedral, and seem to be closely associated with the bloodvessels. They are apparently of connective tissue origin. These authors say the true nature of the body is unknown, but in all probability it is largely true reticulum. A branch of the carotid artery enters the body, breaks up into many smaller branches, one supplying each follicle. The branch of the follicle breaks into a capillary network which unites with a vein at the periphery of the follicle. The body contains many medullated and nonmedullated nerve fibers, fine branches of which go to the follicles. Ganglionic cells are rarely found.

Boehm and Davidoff³¹ say septums, derivatives of the capsule, divide the carotid body into lobules which are in turn again divided into small round masses, "the cell balls," are composed of cellular cords, the elements of which are extremely sensitive to reagents. The cells are round or irregularly polygonal, and separated from one another by a delicate reticulum of connective tissue. The capillaries come in direct contact with the spheric groups of cells. The organ is comparatively rich in nerve fibers, and contains a few ganglion cells.

AUTHOR'S STUDY.

From the investigations I have made, it is not possible to believe that the carotid body is present as often as is generally maintained. In the eight fetuses examined, it was present only once. Three cats, one

guineapig, and one rabbit contained no such structure. In one fetus a cervical ganglion occupied the position of the carotid body, and it was only after careful microscopic examination that the nature of the structure was recognized.

The body was found in the one instance attached to the common carotid artery 6 mm. below the bifurcation on one side, and on the other side it was found lying on the inner aspect of the external carotid, 0.5 cm. above the bifurcation. The attachment in both seemed to be by means of a delicate pedicle. They measured 7 mm. in diameter, were firm in consistency, and grayish-pink in color.

The body is enclosed by a fibrous capsule, the density of which varies at different points. From the capsule a band of the fibrous tissue penetrates the body, separating it into two nearly equal parts; from this main partition others diverge toward the capsule, and separate the halves into lobules. The fibrous tissue appears from a tinctorial point of view to be of two types, the coarser fibers with Mallory's reticulum stain, take the anilin-blue with intensity, while the more delicate strands select the acid fuchsin in a somewhat modified hue—a deep lilac. With van Gieson, the delicate fibers fail to stain, or select the acid fuchsin very faintly.

The fibrous tissue contains many bloodvessels. Many of these present nothing unusual, while others are lined with cells, having large round or oval excentric nuclei that evince no great staining affinity. The cell nucleus reacts to Mallory's reticulum stain in a manner similar to the delicate fibrous reticulum. The protoplasm is not abundant and possesses, with Mallory's reticulum stain, a reaction somewhat similar to that of the nuclei. Every now and then the entire bloodvessel wall is made up of somewhat similar cells. These cells are found, not only in and about the bloodvessel wall, but are also distributed throughout the dense fibrous tissue, especially the lobes already mentioned.

The lobules are composed of collections of cells that have no definite arrangement. In instances they appear separated by a delicate reticulum. In only a few does their disposition simulate gland structure. They are very closely set, making it difficult to outline the individual cells. The cells are large, their protoplasm is abundant, the nuclei are large, as a rule oval, and like the protoplasm, react poorly to stains. Minute bloodvessels can be found in all parts of these lobules. In

TABLE GIVING ATTAINABLE DATA CONCERNING A

No.	Operator.	Patient.	Sex.	Age.	D'ration of disease.	Symptoms.	External relations and appearances.	Ligations
1	Riegner, 1890.	F.	32	4½ years.	Visible pulsation, no inequality of pupils, no flushing of face, expansion not noted, size of hen's egg.	No metastasis adherent to vagus; internal jugular and sympathetic.	All carotids; pharyngeal; internal jugular.
2	Maydl, published in 1886.	M.	28	½ year.	Evident pulsation, no expansion, size of pigeon's egg.	No metastases, hard, encapsulated, in bifurcation.	All carotids; pharyngeal; superior thyroid.
3	Dittel.	Ph. S.	M.	32	Several months.	Pulsations light, skin movable over tumor, last week's growth rapid, size of hen's egg.	Encapsulated, hard, vascular, lobulated; near its small tumor; carotid adventitia infiltrated.	All carotids; internal jugular vein.
4	Gersuny, 1886.	F.	18	Not noted.	Not recorded; size of hen's egg.	Encapsulated; uneven, gray, granular; on section many canals; 3 cm. below mastoid.	All carotids; pharyngeal.
5	Albert, 1891.	M.	35	5 years.	Pure blood on tapping, no expansion, last year rapid growth, size of an apple.	In bifurcation; encapsulated, dark red, vascular, lobulated; recurrence in 1 year.	External carotid.
6	Maydl, 1893.	J. R.	F.	46	16 years.	Visible pulsation, murmur over tumor, no expansion, painful recently, size of hen's egg.	Adherent to jugular; carotid's media infiltrated; metastasis; encapsulated, hard, vascular.	All carotids; pharyngeal.
7	Maydl, 1895.	M.	34	4 years.	Pulsation ceases upon compressing carotid, systolic murmur; recently it inconveniences him.	Enlarg'd lymph node near tumor; carotid wall not infiltrated.	Common, internal, external carotids; pharyngeal; superior thyroid.
8	Heinleth, 1900.	M.	60	Noticed after extraction of a tooth, site in the bifurcation of common carotid.	Tumor encapsulated and lobulated.	Tumor removed without any ligations.
9	Malmcoosky, 1899.	F.	10 years.	Skin free, fremitus over tumor pulsation, bruit synchronous pulse in temporals, growth rapid in last year.	Surface smooth.	Common, external, internal carotids; internal jugular.
10	Siniouschine, 1901.	F.	8 years.	Growth slow, recently pain in ear, skin free, tumor soft, movable side-wise, size of walnut.	Common, internal, external carotids; internal jugular vein.

Nerves injured.	Microscopic appearance.	Clinical diagnosis.	Pathologic diagnosis.	Results.	References.
Vagus and sympathetic.	Alveolar structure, each alveolus is bounded by a structure that contains a capillary; alveolus has cells.	Lymphoma.	Whether of endothelial or perithelial origin Marchand does not say, but is malignant.	Died of bronchopneumonia.	Reported by Marchand, Festschrift für Virchow, Bd. I, 1891.
	Periphery is alveolar; alveoli contain polygonal cells; center more fibrous tissue and pigment.	Lymphoma.	Paltauf says perithelioma of carotid gland.	Postoperative hemiplegia and aphasia; in 4 years no return.	Allg. Wien. med. Zeitsch., 1886; Paltauf, Ziegler's Beiträge, 1892, Bd. xi.
	In periphery columns and cylinders of cells, blood; spaces lined by endothelium; center fibrous, contains few cells.	Not made.	Same as above.	Died of secondary hemorrhage.	Paltauf, Ziegler's Beiträge, 1892, Bd. xi.
Paralysis of the left vocal cord.	Cell cylinders conspicuous; degenerated blood and cells in the alveoli; pearl-like in alveoli; like endothelioma.	Tuberculous lymph-node.	Same as above.	Paralysis of left vocal cord; no return in 4 years.	Same as above.
	Similar to the last but presents hyaline degeneration.	Not made.	Same as above.	Cured, removed again 1 year later.	Same as above.
Sympathetic.	Stroma and alveoli, oval cell in the alveoli, numerous blood-vessels; hyaline degeneration of stroma and alveolar walls.	Carotid tumor.	Endothelioma.	Cured; mydriasis marked but stationary.	Kopfstein, Wien. klin. Rundschau, 1895, Bd. ix.
Vagus, sympathetic, hypoglossus, facial.	Same as No. 6; structure of lymph-node like tumor proper.	By exclusion intercarotid tumor.	Malignant; does not state definitely; says similar to No. 6.	Cured; aphonia, paralysis of left vocal cord.	Kopfstein, Wien. klin. Rundschau, 1895, Bd. ix.
None.	Cell groups enclosed by fibrous bands, between groups are capillaries with thin walls; tumor cells derived from capillaries.		Perithelioma of carotid gland.	Cured.	Heinleth, Centralblatt für Anat., 1900, Bd. ix.
Removed 8 cm. of pneumogastric.	What were first thought to be lymph spaces are blood vessels; cell proliferation from external portion of the wall.	Lymphosarcoma of the carotid sheath.	Perithelioma of the carotid gland.	Cured.	Malmöosky, Review, 1899, Contrib. à l'étude des tumeurs de la gland carotid.
None.	Excentric development, cannot tell whether cells are derivatives of endothelium or perithelium.	Fibrolipoma.	Unable to say whether endothelial or perithelial.	Cured.	Seance, 401, de la Soc. de Chir. de Moscou, 1901.

most instances their walls are barely perceptible, but they are, nevertheless, nearly always present. Every now and then one is found that apparently penetrates a large cell, but even then a delicate wall can be made out. There appears to be an intimate relation between these cells and the bloodvessels, just how they are related I cannot from my present studies say. I am strongly of the opinion that these lobules are produced by the proliferation of the endothelial cells of the bloodvessels. The encroaching cells give rise to the apparently delicate wall observed. The sections examined contained neither multipolar cells nor nerve fibers.

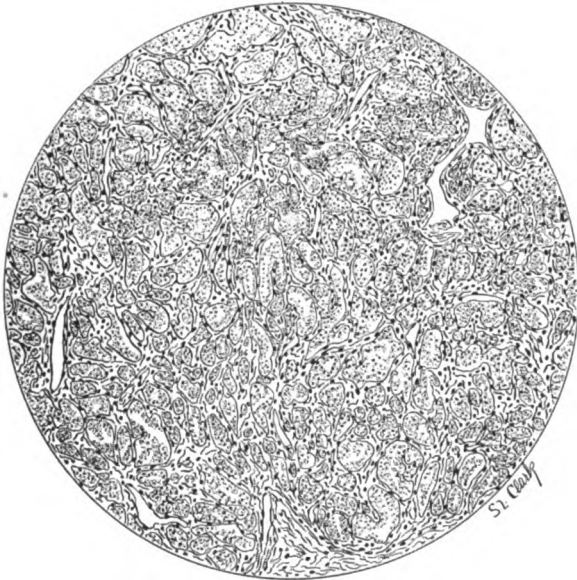
EMBRYOLOGY OF THE CAROTID BODY.

Luschka believes the carotid body develops from the endoderm. In an embryo of 14 weeks, Valentine found the carotid gland present on both sides; its shape, firmness and connecting filaments were the same as in the fully developed organ.

Stieda,²¹ in embryos of 11 mm., found a round body no longer connected with the epithelium of the pharynx nor of the thymus and regards it as the interglandula caroticum. Katschenko²² says the structure from which Stieda believes the carotid body develops corresponds to the so-called Katschenko's thymus ganglion. He finds an ellipsoidal body on the internal carotid, at the bifurcation, in embryos of 14 mm. and 18 mm. The thickening adventitia is pushed to one side and later toward the bifurcation; at the same time many vessels, arising from the internal carotid, enter the body. Fischelis,²³ on the other hand, regards the glandula caroticum as originating from the tissue lying between the approximating ectodermal and the endodermal layers and does not consider the organ as developing from epithelial structure. Pierre de Meuron²⁴ believes the carotid body develops from the third branchial cleft. In sheep, the organ referred to is found near and above the bifurcation of the carotid although in embryos of 18 mm. it is not separated from the thymus. Rabl,²⁵ in mammifera and in birds, found the endoderm of the third cleft furnished the ventral diverticulum for the thymus and the dorsal bud for the intercarotid. Paltauf concurs in the view expressed by Katschenko.

Van Bemmelen,²⁶ in snakes, saw the retrocarotid corpuscle develop at the expense of the endoderm of the third cleft. Prennant,²⁷ after studying the opinions already given, concluded that the retrocarotid gland

develops in the form of an epithelial bud at the expense of the endoderm of the third branchial cleft. Princeteau, from its position and relation to the common carotid, looks upon the origin as being in common with that of the common carotid which develops from the third branchial arch. Borst²⁸ says the carotid body originates from the mesenchyme. Heinleth believes the first indication of its development is a cellular thickening of the primitive carotid at its posterior and outer periphery.



Tumor of carotid body. Leitz, 24 mm.; oc., A. Reduced one-half.

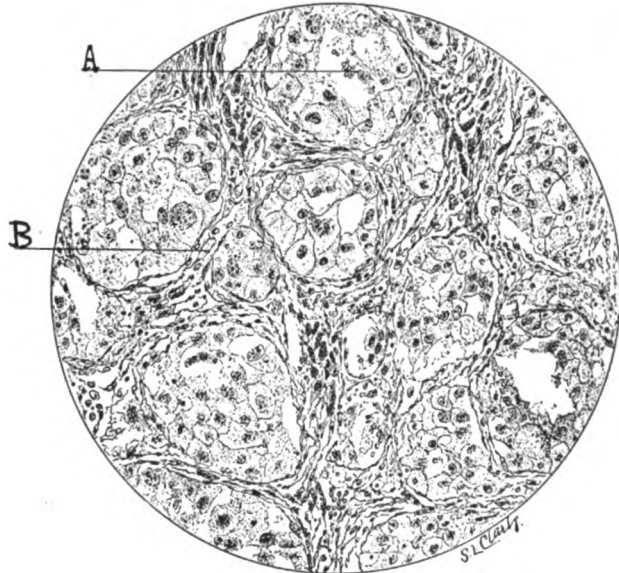
Kohn thinks the carotid body develops from the embryonal ganglion cells of the intercarotid plexus.

TUMORS OF THE CAROTID BODY.

CASE.*—F. J. R., aged 48, mechanic. Six years ago the patient first observed a growth just below the angle of the inferior maxilla and in the anterolateral part of the neck. It grew slowly but apparently continuously; it did not inconvenience him in the slightest degree. During these six years he has gained in weight.

* For the use of the clinical notes in this case I am indebted to Professor Hearn, of Jefferson Medical College, who operated upon the patient

Examination reveals a tumor that extends from the angle of the right inferior maxilla 2 cm. below the upper border of the larynx along the anterior border of the sternomastoid muscle. The outline of the tumor is indefinite to inspection; from its most elevated portion which is 5 cm. to the right of the median line on a level with the superior border of the larynx it merges gradually into the surrounding structure; upon palpation, however, the outlines of the growth are definite; it is firm, about 7 cm. by 4 cm. in diameter, and not attached to the skin, it is freely movable from side to side but not vertically. There



Perithelioma of carotid body. Obj. B. and L., $\frac{1}{8}$ inch; oc., 1 inch. Reduced one-half. A, red blood cell in an alveolus; B, blood vessel in the stroma between alveoli.

was present neither pulsation nor expansion; the pupils were equal and the face was not flushed.

At the operation which was performed by Professor Hearn at Jefferson Hospital, the growth was found firmly attached to the common, internal, and external carotid arteries and internal jugular vein. Bleeding from the tumor was profuse. In attempting to dissect the neoplasm from the vessels, the jugular vein, the external and internal carotid arteries were torn: this accident necessitated the ligation of the common carotid below, the internal and external carotid above and the internal jugular vein above and below the growth in order to complete its removal.

For several days after the operation the patient could not speak above a whisper. He gained strength slowly but left the hospital eight days after operation. In a short time he began to complain of headache, especially in the median parietal

region; then it was noticed that he became irrational for short periods only; there were no other symptoms to indicate a tumor of the brain. Soon after leaving the hospital he began to lose flesh rapidly, he complained of fatigue. There was no evidence of recurrence at the original site of the tumor nor at any other point. He died of cerebral anemia nine weeks after leaving the hospital.

Microscopic Examination of the Tumor.—The specimen consists of an irregular mass measuring 5 cm. by 3 cm. by 3 cm. It is dark red, soft and encapsulated. The capsule for the most part is smooth and glistening. The specimen cuts with ease, the incised surfaces are dark red, granular and contain many small cavities filled with blood.

The tissue was fixed in Bensley's fluid, embedded in paraffin, sectioned and the sections stained with hematoxylin and eosin, by Van Gieson's method, for elastica by Weigert's method, with Mallory's reticulum stain, with iron-hematoxylin, for myelin sheaths by Weigert's methods and for ganglion cells by Nissl's method.

Histology.—(See Figs. 1 and 2). The sections present an alveolar arrangement. The capsule is comparatively thick, composed of dense wavy fibrous tissue and contains a few lymphoid cells. From the capsule, bands of fibrous tissue penetrate the tumor giving support to the structure and, by division, form alveoli of a fairly uniform size separated by this stroma-like tissue; the fibrous septums thus formed are fairly constant in thickness and structure, although at points the fibrils are coarsely grouped and in not a few areas they are the seat of a hyaline degeneration. The alveoli are occupied by cells that are oval or round and measure from 15 to 20 μ in diameter. The nuclei are large, round or oval and stain with a moderate degree of intensity; the oval nuclei stain deeper than the round. The protoplasm is abundant, granular, and reacts to its selective stain with a fair degree of intensity. In some alveoli the cellular contents are closely packed, the cell outline indistinct and the grouping irregular; in others the cells are less crowded and there is a suggestion of tubular arrangement. In a few alveoli there are besides these cells a number of erythrocytes. Only now and then can an intercellular reticulum be demonstrated. The walls of the alveoli are thin and in many instances vessels appear to course in them, most often in the center of the wall, but every now and then vessels are seen lying very close to the alveoli, being separated from them by delicate strands of tissue only. There is no difficulty in demonstrating red blood cells in these vessels.

Elastin was found in the bloodvessels only. Nerve fibers were not found and ganglion cells were also absent. The bloodvessels were large and abundant in the supporting structure of the tumor, and were filled with blood.

Diagnosis.—Since in many places the bloodvessels can be seen in the alveolar walls and at times separated from the alveolar contents by a delicate strand of tissue, the supposition that the tumor cells are derivatives of perithelium is entirely reasonable. I am therefore, favorably impressed with the term "perithelioma."

Etiology.—These tumors occur especially in adolescence and in adult life. In the cases reported the youngest patient was 18 and the oldest 60. Neither

sex seems predisposed; in the collated cases there were eight females and six males; in one of the reported cases the sex is not given. In two cases there was a history of malignant disease in the family. One of the tumors was first noticed after the extraction of a tooth and fracture of the inferior maxilla; this patient had a history of inflammation of the throat and glandular swelling. In another patient there was a history of tonsillitis. One of the tumors was first observed after confinement. Heinleth explains the formation of these tumors as follows: The carotid body develops until the age of puberty, when it either atrophies or the development is arrested; if the body continues to grow a tumor is formed.

Symptoms.—They are not varied, but more or less constant. The tumor is insidious in its onset, slow in its growth, but later it may develop rapidly, when for the first time the patient consults a surgeon. Reclus says the tumors are seen early in those patients who present themselves to the surgeon for cosmetic purposes. He further observes that Maydl has operated upon three of these tumors in nine years, and therefore the neoplasms cannot be regarded as being extremely rare. There is always a history of long-standing growth. Maydl saw his first case six months after the appearance of the tumor and the second 16 years after it was first noticed; as a rule the patients come to the surgeon five or six years after the tumor is first observed. The growth of the neoplasm is slow during the first few years, but later usually becomes more rapid, at which time the patient seeks the advice of a surgeon. In these later stages the tumor may become painful and present other distressing symptoms; in Cuneo and Dainville's case there were lancinating pains radiating into the ear, associated with difficulty in swallowing, miosis of the right eye and vasomotor disturbances of the face. In Scudder's case the tumor became larger and tender when the patient caught cold; in one of Maydl's cases tinnitus developed just before he saw the patient. In the collated cases eight presented evident pulsation, in three there was no pulsation, in four there was no note of its presence or absence. In no case was there expansile pulsation. The pulsation is not caused by blood entering the tumor, but is due to transmission from the carotids. The skin is never attached to the growth. The neoplasm is movable sidewise but not vertically. As a rule a murmur is heard over the tumor. Reclus

says the systolic tone is not more intense than over the common carotid. By pressure the tumor may be made to disappear; this disappearance is not due to the evacuation of the blood content, but rather to a displacement of other organs. Pulsation is synchronous in both temporals.

Diagnosis.—First, the position of the tumor, anterior to sternomastoid muscle, extending from the superior margin of the thyroid cartilage to within a few centimeters of the angle of the jaw; the evident pulsation, but no expansion; the murmur over the growth, but of no greater intensity than over the carotid artery; the synchronous pulsation in both temporals; the boggy or elastic character of the tumor; the movable skin over the growth; a history of long standing and of slow enlargement; in the few months prior to the time the patient presents himself to the surgeon the growth usually has been rapid; occasionally there are vasomotor disturbances, as flushing of the face and inequalities of the pupils. Of the collated cases, only one patient was tapped, and this was followed by a flow of pure blood. There is no constant predisposing condition.

These tumors have been mistaken for tuberculous lymph-nodes, lipoma, fibrolipoma, lymphosarcoma aneurysm, and aberrant thyroid; upon superficial examination, cystomas of the neck may be mistaken for tumors of the carotid body.

Reclus says tuberculous lymph-nodes are entirely hard or entirely fluctuating and multiple. As a rule, these nodes involve the surrounding structure and may be tender; lipomas are more superficial, are softer, and less consistent; although fibromas are harder than the carotid tumor, and are rarely found at this site, yet should they develop here, it would be very difficult to differentiate them from the carotid tumor. According to Kopfstein, pulsation and murmur rule out lymphosarcoma. Reclus observes that lymphosarcomas are hard, malignant, everywhere adherent, and of rapid growth. Absence of expansion rules out aneurysm; Kopfstein fortifies exclusion by the absence of syphilitic infection and atheroma in his case. The same author excludes aberrant thyroid by the absence of an enlarged thyroid gland; Reclus says he has never seen an aberrant thyroid as high as the thyroid cartilage. Cystomas of the neck are superficial, fluctuating; tapping gives either a light straw-colored or clouded fluid; as a rule, they are congenital.

Although Borst and Reclus say these tumors are benign, Marchand and Kopfstein state definitely that the tumors in their cases were malignant. Paltauf notes the recurrence of the tumor in one of his patients a year later. While I am inclined to look upon these tumors as malignant, I believe that in the case reported in this article the patient died of cerebral anemia rather than as a result of the neoplasm itself.

Reclus stands alone in questioning operative interference. He says if we consider that these tumors are benign and recognize the dangers incident to their attachment in this operative field, it is better to let them alone until they produce symptoms which are dangerous to life.

A table of reported cases is appended.

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CARCINOMA OF THE ESOPHAGUS.*

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Tumors of the esophagus are not of common occurrence. Of the benign neoplasms, fibroma is the most frequent; it may be in the submucosa, interstitial or polypoid. Rarely the polypoid or pedunculated fibroma is so situated that it may be vomited or regurgitated into the pharynx and give rise to symptoms of suffocation, relieved by swallowing. Rokitsansky¹ reported a smooth, lobulated fibroma 7 in. long and 2½ in. wide. Sarkisoff² reports a fibroma of the esophagus that underwent necrosis and was vomited; the patient recovered. He thinks the tumor was located near the sixth dorsal vertebra. A few cases of myoma, lipoma and adenoma of the esophagus have been recorded. Such tumors, however, are very rare.

Howard³ reports a primary sarcoma of the esophagus with metastases to the cardiac end of stomach. In individuals under 25, sarcoma is more common than cancer. It usually involves the lower third of the organ. Of the 12 reported cases of sarcoma of the esophagus, most were in males; 9 of the 12 were in the lower half of the organ; the tumor usually surrounds the lumen, but in 3 cases it was pedunculated or polypoid.

There were symptoms of obstruction in 11 of the 12 cases; perforation or involvement of respiratory organs occurred in 4. All varieties of sarcoma except angiosarcoma have been reported; 25% are of the round-cell variety. Metastases were present in 5 of the 12 cases and in 2 the metastases were widespread. Sarcoma of the esophagus runs a more rapid course than cancer. Since the publication of Howard's paper, v. Eicken⁴ has reported a spindle-cell sarcoma of the esophagus.

Carcinoma of the esophagus is usually regarded as rare even when compared with cancer of other parts of

* From the Laboratories of the Jefferson Medical College Hospital, and the Philadelphia Hospital. Read before the Philadelphia Pathological Society, April 14, 1904.

the body. Of 7,290 cases of cancer collected by Williams, 2,669 were in men and of these 5.3% were primary in the esophagus. Of 4,628 cases of cancer in women, the primary lesion was in the esophagus in 0.7% (35). Kraus⁶ does not think cancer of the esophagus so rare as usually is held; he gives the esophagus about the fifth place among the organs in which carcinoma occurs. Tanchon⁷ in 9,118 cases of cancer, found 18 of the esophagus and 2,303 of the stomach.

Although a disease of advanced life, it is not unknown in the young; Heiman⁷ recorded a case in a patient of 19, Stewart⁸ in a patient of 23, and Harris⁹ in a man aged 21. Most patients have passed 40, and 35% of them are between 50 and 60. The great preponderance of patients is males; of 772 cases of esophageal cancer collated by Kraus, 584 were in males; but 12 of Butlin's¹⁰ 59 patients were women; Rolleston¹¹ states that of 55 cases of carcinoma of the esophagus collected by Wilson from the postmortem books of St. George's Hospital, 8 were in women, and of 510 cases gathered by Newmann, 108 were in women; women are attacked earlier in life (about forty-fourth year) than men (about fifty-fourth year) (Butlin); of Emanuel's 6 cases, 5 were in men between 51 and 55 years and 1 in a woman, aged 33.

The exciting cause of cancer of the esophagus, like cancer in general, is as yet not known. Many predisposing factors have been given more or less importance, some of them clearly more than they deserve. In this article it is not my purpose to include cancer of the esophagus resulting from metastasis or direct extension, but mention should be made of those rare cases of esophageal carcinoma resulting from involvement of the organ by tumors arising in the pharynx, tongue or stomach. That trauma or irritation of some kind may have something to do with the development of esophageal cancer is indicated by the fact that such growths are most frequent where the organ is most exposed to insults from bodies during their transmission through its lumen. Zenker¹² thinks it may depend on chemie, thermal, or mechanical irritation. All writers lay some stress on alcohol as a possible cause. Körner¹³, Voelcker¹⁴ and Leberts¹⁵ suggest that it is favored by the mechanical irritation resulting from enlarged periesophageal or peribronchial glands. Ritter¹⁶ thinks an esophageal diverticulum may constitute a point from which cancer can arise. Henoeh¹⁷, Kraus¹⁸, Deininger

and others attribute a certain influence to hot foods or bolting large boluses. Wendland¹⁹, Fritsche²⁰ and others have implicated hot or cold draughts. Ritter²¹ thinks a traction diverticulum may constitute a point of lessened resistance in which carcinoma may arise. It is easy to appreciate that any pouch or "silent area" in which food could lodge or other irritants prolong their action, might be similarly disposed. Leberts found a plum seed in a carcinoma and suggests that such foreign bodies may be causes. Röpke²² reports an esophageal carcinoma developing out of a scar. Wolf²³ reports two cases of carcinoma of the esophagus associated with spondylitis deformans, and briefly records a third case observed by Orth, and states that Schmorl knew of two additional cases.

With regard to location, authorities are not agreed. J. Solis-Cohen²⁴ does not think that any particular division of the esophagus is especially prone to the disease. Recklinghausen taught that cancer of the esophagus was most common where the organ is crossed by the left bronchus. Similar views were held by Virchow²⁵, Harrison Allen²⁶, Zenker²⁷, and Klebs, Rindfleisch, König and some other textbook writers. In 901 cases collated by Kraus²⁸ 44 involved more than one part of the organ; 397 were in the lower third, 302 in the middle and 158 in the upper third. Von Hacker in 181 cases found 13 in the neck region, 53 in the neighborhood of the bronchial bifurcation, 36 in the hiatus and 29 at the cardia, making the numbers for the various thirds, from above downward, 13, 53 and 65, respectively. Butlin observes that if the esophagus be divided into upper and lower halves the tumors will be fairly equally distributed in the two parts. In Newmann's²⁹ 445 cases, 227 involved the upper part of the esophagus; 120 were situated in the lower and 98 in the middle third. According to Gross³⁰ the most frequent site is behind the larynx; Osler³¹ says the upper third, and Pepper³² in order of frequency, names the region of the cardia, bronchial crossing, and cricoid area; Zenker and v. Ziemssen agree with Kraus and v. Hacker.

With regard to the type of cancer all records show that squamous-cell epithelioma is by far the most frequent; other types of carcinoma of the esophagus are exceedingly rare. Butlin's cases consisted of 54 squamous-cell, 3 scirrhous, 1 medullary and 1 colloid. The colloid spoken of by Butlin, and one observed by Eppinger³³ are exceptional. The adenocarcinomas are usually

at or near the cardia ; they may be extensions from primary growths in the stomach or possibly some of them arise from ectopia of gastric glandular elements abnormally placed in the lower part of the esophagus. Of the origin of esophageal cancer from glands in the mucosa too little is known to justify any sweeping deductions.

Anatomically cancers of the esophagus assume many forms. Papillary growths, irregular projections, polypoid masses that may or may not be lobulated, bossed or fissured, infiltration of the wall of the tube tending to encircle, but rarely doing so, and irregular linear masses which may or may not ulcerate, constitute the most common forms. Kraus cites cases in which all but a few centimeters of the tube were involved ; in other cases, as in the one reported in this paper, large nodular masses develop attached to the esophageal wall by relatively narrow stalks ; this type ulcerates slowly. It may give rise to marked obstruction that disappears with the advent of necrosis even before destructive ulceration approaches the esophageal wall. This misleading clinical phenomenon is particularly remarked upon by Arnold.³³ Ulceration was absent in but 5 of 54 in Butlin's series and in 3 of the 55 St. George's Hospital cases. Isolated patches of ulceration occur. In types not taking on this polypoid character or having assumed that form and later by necrosis lost the external projection and finally invaded the esophageal wall, stenosis may be brought about by infiltration or, what is more common, the coincident increase in fibrous tissue associated with contraction may narrow the tube. As a result of the obstructive lesion there is commonly an initial hypertrophy of the esophageal musculature sooner or later followed by wasting and dilation. The more or less relaxed organ may assume a spindle form but usually the cavity created by gradual distention is largest just above, but not immediately at, the obstruction and from this point of maximum width progressively narrows to approximately the normal size at the upper limit of the organ. Of course the lower the tumor and, other things being equal, the slower stenosis develops, the more capacious the sac may be. In some instances fluids and solids may accumulate in such quantity that the consequent regurgitation appears, from necessity, to be a true vomiting of gastric contents. Such dilation may occur without demonstrable stenosis at autopsy, but, as Rolleston indicates, the differences between functional obstruc-

tion and demonstrable anatomic narrowing may be quite marked.

Some of the complicating anatomic changes are of great clinical interest. Cancer of the esophagus tends to involve the peribronchial and mediastinal lymph-nodes, the gastric glands, the air passages and adjacent blood-vessels and lungs, the thyroid and, less frequently, the pleura, pericardium and heart. When the lung is penetrated Rolleston observes that it is usually the right organ that is involved.

Treves²⁴ reports a case of carcinoma of the lower end of the esophagus involving nearly the whole length of the lesser curvature, the patient surviving a gastrostomy (at which time the diagnosis based on symptoms was verified) for 2 years and 11 months. Fütterer²⁵ reports a case in which cancer of the stomach depended upon transplantation from a growth in the esophagus. He collected six similar cases from literature. Kraske has reported two instances of cancer of the rectum with transplantation below. When the esophagus is perforated by the growth, the trachea may be involved; in Zenker's 120 cases of perforation the air passages were affected in 70; in 26 one bronchus, and in 21 the trachea was entered; in 17 the right lung and in 6 the left lung was affected. In Homan's²⁶ case there was an external opening and also perforation of the trachea.

Adenot and Cadet²⁷ report cancer of the esophagus with esophagotracheal fistula and gaseous distention of the stomach by air, thought to have passed through the trachea into the esophagus, and in that way into the stomach. Gastrostomy was done, at which time the stomach was found distended, and the organ filled and emptied during respiration in such a way as to render the operation more difficult. Three centimeters above the tracheal bifurcation exactly in the median line posteriorly, there was a mammillated projection into the trachea that contained an opening communicating with the esophagus. Sirot²⁸ has been able to collect 68 cases of esophagotracheal fistula. Adenot and Cadet do not state whether these were all cancerous or not and the original paper has not been available for examination. Since the publication of Sirot's thesis a number of cases has been reported; the complication is not infrequent. In nearly all cases of cancer of the esophagus in which the stomach has been observed, at operation or autopsy, the organ is small, retracted, hidden under the liver, difficult to find, and, at operation, surgeons have opened

the colon instead. Adenot and Cadet think that in their case during inspiration, air passed through the fistula into the esophagus, and in expiration it was forced onward into the stomach where it accumulated. They therefore hold that when a tracheoesophageal or bronchoesophageal fistula is suspected, the stomach should be percussed with care, to determine if there is any undue distention of the organ caused by aerophagy. Cade and Revol³⁰ and a few other observers have reported cases in which esophagotracheal fistulas secondary to cancer of the esophagus were entirely latent.

Ross⁴⁰ reports a cancer of the esophagus involving the vertebrae and producing paraplegia.

Bureau⁴¹ reports a cancer of the esophagus, adherent to the left auricle in which was a nodule, the size of a pea, situated just under the endocardium. There was a stenosing growth of the esophagus with ulceration and perforation into the middle lobe of the right lung. The sputum was fetid, and a pleural effusion amounting to 500 cc. was present. The patient had vomited some blood on one occasion. The muscle fibers of the heart were atrophied and infiltrated by cancer cells; the left pulmonary vein and the pneumogastric were compressed by the growth which was an epidermoid cancer. Tachycardia (160) was present.

McKendrick⁴² records an epithelioma of the upper part of the esophagus with involvement of the pneumogastric, and including both recurrent laryngeal nerves; the symptoms—slight dysphagia, dyspnea, stridor, cough, and aphonia—indicated aneurysm of the aorta. Kuckein⁴³ reports two similar cases, both diagnosed as aortic aneurysm and in both expansile shadows by the röntgen ray were produced, due to the pressure of the filling aorta upon the tumor.

Saundby and Hewetson⁴⁴ report an extensive carcinoma of the esophagus occurring in a man aged 50. He had been ill two years. There were enlarged glands in the neck and around the aorta, the latter involving both vagi and the recurrent laryngeal nerves; edema of the lungs, consolidation, and secondary deposits at the base were also present. The upper part of the esophagus for six inches was involved in a sloughing malignant growth, which projected into the lumen and bound the esophagus to the trachea, which at one point was perforated. The growth extended from the first ring of the trachea to two inches below the bifurcation—a distance of six inches. The lumen of the esophagus between these

points was three times the normal size; there was no stricture at any point. The growth extended completely around the esophagus and over points involved the whole thickness of the wall. The broncholympathic glands were affected. The trachea was compressed, and a button-like mass extended into the left bronchus. The pneumogastric nerves were involved on each side just behind the bronchi. The growth was a spheroidal-cell carcinoma; cell nests were absent in both primary and secondary growths. The difficulty in swallowing depended not upon stenosis, but involvement of the musculature of the esophagus. Fluid gravitated into the stomach better than solids; hence the appearance of stenosis. The sudden attacks of vomiting appeared to depend upon involvement of the pneumogastric nerves.

The tendency of such tumors, when located in appropriate regions, to involve, usually by inclusion, any adjacent nerves may account for the occurrence of bradycardia or tachycardia, both of which have been observed repeatedly. Compression of a degree sufficient to stimulate the pneumogastric would slow the heart and stimulation of the fibers coming from the inferior cervical sympathetic ganglion would accelerate, and possibly in these facts may be found a satisfactory explanation for the occasional tachycardia and bradycardia. The latter was present in Arnold's case, the pulse, for two months, ranging between 50 and 60.

Carcinoma of the gullet may be latent; Hödlmoser⁴⁶ reports two such cases. In both dysphagia was absent, and there were no esophageal symptoms. Unilateral paralysis of the recurrent laryngeal nerve was the most marked symptom. Some enlargement of the subclavicular glands was present, and in one case the tumor was attached to a tuberculous gland.

Emanuel⁴⁷ records six cases of cancer of the esophagus without obstruction. In two of his six cases infiltration and perforation of the trachea occurred; in three the left bronchus was perforated; in one case the growth was low and penetrated the lung. Cough or other respiratory disturbance coming on immediately after swallowing should be regarded as a symptom of laryngeal or bronchial involvement.

Dickinson⁴⁷ reports a case in which penetration of the subclavian artery occurred; S. Jones⁴⁸ records an instance of perforation of the intercostal arteries with fatal hemorrhage. Taylor⁴⁸ has been able to collect nine cases of ulceration into the aorta or its branches.

With regard to the life expectancy in these cases, much depends upon the intervention of the surgeon, who may, by gastrostomy, prolong life. Rolleston states that most patients die within a year of the appearance of symptoms, that carcinoma of the upper part of the esophagus is more rapidly fatal than when the lower third is involved, and scirrhus carcinoma progresses less rapidly than the squamous-cell variety. The last statement is not in harmony with our knowledge of the two varieties of cancer when occurring elsewhere. Pepper's observation that metastasis is less frequent than in carcinoma of other organs is correct, if we exclude certain feebly malignant epitheliomas involving the skin.

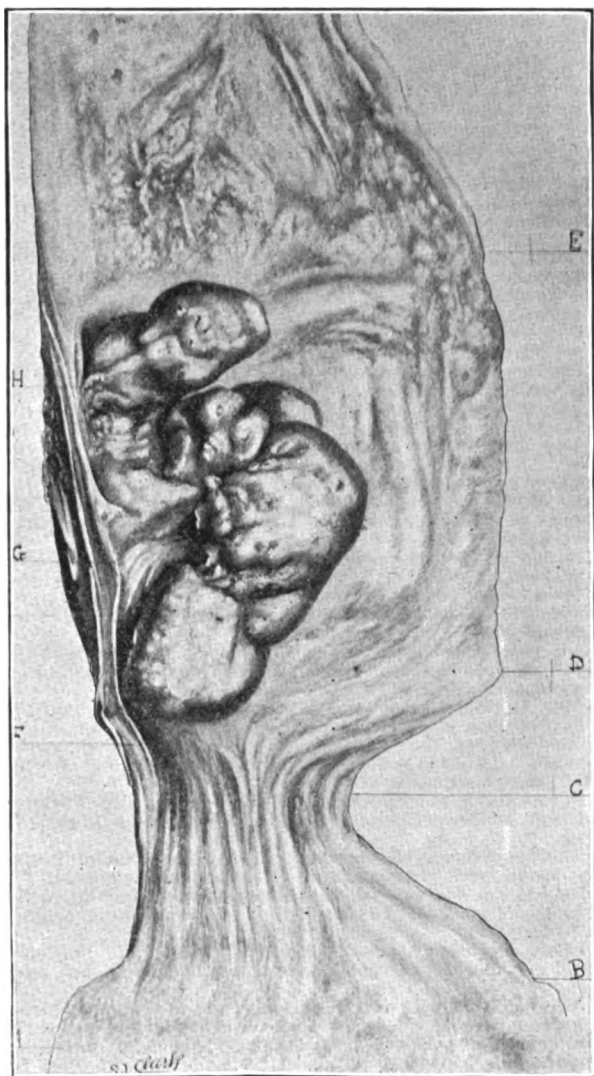
Diagnosticians will find no little difficulty in differentiating esophageal malignant stenosis from other forms of narrowing, and these difficulties will not be lessened by the findings of Soupault,⁵⁰ who records four cases in which the symptoms resembled stricture of the esophagus, but were due to atrophic retraction of the stomach, small retracted organs being found at autopsy; four similar cases are found in literature. Von Cackovic⁵¹ reports two cases of total contraction or shrinking of the stomach. In such cases the symptoms and even the results of instrumental examination may closely resemble stenosis, and hence carcinoma of the esophagus.

With regard to the treatment little can be said. Radical operative procedures directed to the neoplasm have proved disastrous, but gastrostomy or other palliative undertaking usually is regarded as most valuable. Recently Exner⁵² has treated esophageal cancer by the use of a tube of radium attached to the end of an esophageal bougie; the capsule containing the radium should have the diameter of a No. 16 bougie. He reports three cases, in all of which there was lessened stenosis, but as this may result from sloughing independently of any so-called resorptive action, the observation offers at present no conclusive evidence of specific benefit.

The following is a brief summary of the postmortem findings in a case of carcinoma of the esophagus coming to autopsy in the Philadelphia Hospital. The patient was under the care of Dr. Thomas G. Ashton, who will report the clinical details elsewhere:

H. McG., Men's Medical Ward. Patient, male, white, 63 years, native of Ireland. Admitted August 27, 1903; died January 26, 1904; autopsy held January 26, 1904.

Pathologic Diagnosis.—1. Visceroptosis. 2. Chronic adhesive pleuritis (sinistra). 3. Healed-in pulmonary tuberculosis. 4. Atrophy of heart. 5. Arteriosclerosis. 6. Chronic intersti-



Squamous-cell carcinoma of the esophagus of the polypoid type. A, cardia of stomach. B to C, cardia of esophagus. C, hiatus esophagi. D to E, area of maximum dilation of the esophagus; from E upward the organ gradually diminishes in size. F, wall of esophagus. G to H, pedicle of tumor by which are attached the projecting bosses of the newgrowth; at the base there appears to be but slight infiltration beneath the submucosa, although the esophageal wall is slightly thickened. The line F, G, H is near the midline posteriorly from which the tumor has arisen.

tial nephritis. 7. "Polypus" of esophagus. 8. Catarrhal gastritis. 9. Atrophy of liver. 10. Meckel's diverticulum.

Body is that of an emaciated, aged male; marked atrophy of the muscles; scaphoid abdomen; over acromial end of both scapulas are endosseous nodes irregular and plate-like extending downward along the spines. Subcutaneous fat is scanty, almost wanting. Musculature pale, flabby, wasted.

Abdomen, marked visceroptosis; all of the small intestine lying in the pelvis, transverse colon on brim of pelvis. Duodenum just under umbilicus. Liver also prolapsed. Stomach nearly vertical.

Thoracic cavity. Left pleura uniformly adherent with old firm, fibrous adhesions. Right pleura adherent only at the base posteriorly.

Pericardium contains 100 cc. of clear, straw-colored fluid. Serosa normal. Subepicardial fat is gelatiniform.

Right ventricle contains small quantities of coagulum. Right auricle capacious and distended with clots. Left side empty. Auriculoventricular orifice on right side dilated, admits four fingers and thumb. Valves of right side normal. Marked thickening of mitral leaflets. Atheroma of valve bases. Aortic leaflets slightly stiff; no marked valve lesions. Coronary arteries tortuous, typical pipestems at places. Atrium of left coronary artery stenosed. Myocardium brownish, firm, contains small grayish areas. Heart weighs 250 gm. Aorta atheromatous.

Lungs: Both organs show same changes; a few old cretaceous areas 0.25 cm. by 0.5 cm. in diameter. Similar changes in peribronchial glands. Bronchi normal. Larynx and trachea show no gross lesions. Left lung weighs 500 gm.; right lung weighs 520 gm.

Spleen normal in size and color; slightly fibrous; contains numerous cretaceous nodules 2 mm. to 5 mm. in diameter. Parenchyma slightly edematous and somewhat congested. Malpighian bodies rather inconspicuous. Weight, 120 gm.

Left adrenal slightly enlarged; contains many small cretaceous tubercles. Left kidney: Cortex narrow, firm, capsule adherent, surface granular, resists incision, considerably congested, but not small in size.

Pelvis and ureters normal. Right adrenal and kidney in condition similar to the left. Right kidney weighs 150 gm.; left, 160 gm.

Bladder contracted and empty. Middle lobe of prostate slightly enlarged. Internal and external genitals normal.

Duodenum normal. Biliary passages patulous. Gallbladder distended with 250 cc. of rather thick bile, containing considerable biliary sand.

Liver slightly fibrous; capsule thickened; adhesions around gallbladder. Organ rather soft and flabby, but resists incision. Weight, 1,570 gm.

Esophagus: On opening pericardium a fusiform mass is recognized presenting on posterior wall. Pericardial surface smooth and movable over mass. No evidence of pressure on bronchi, though slightly adherent to both trunks; aorta free. On removal of chest viscera the fusiform enlargement of esophagus is better seen. It begins 2.5 cm. above the cardia, attains a maximum width of 4.5 cm. at a point 10 cm. higher. The esophagus incised on its anterior surface. Four centimeters above the cardia is found an irregular polypoid mass made up of numerous bosses, and extending in the axis of the

esophagus 9.5 cm. The point of attachment of lower end (pedicle), however, is 5.5 cm. from the cardia, and extends upward 8 cm. This pedicle seems to be about 2.5 cm. in width, its accurate width cannot be determined without mutilation of the specimen. The new growth is composed of bosses varying in size from 4 mm. to 5 mm. in diameter, to larger mass 5 cm. in maximum diameter. (See illustration.) At the upper end is an ovoid, almost free polypoid mass, 2.5 cm. by 1.5 cm., intensely congested, and at one point shows beginning necrosis. The esophagus at the cardia measures 4 cm. in circumference; 2 cm. above this point (hiatus oesophagi) is a slight constriction, measuring 3 cm. in circumference. Just over the mass the esophagus seems to be widest, measuring 9.5 cm. in circumference. Just above mass, 12 cm. from cardia, the esophagus measures 8 cm. in circumference, from which point it gradually narrows to what seems to be normal lumen (4 cm. in circumference) 22 cm. above cardia. The esophageal wall seems fairly thick, but rather irregularly so, 0.25 cm. in thickness at the cardia, 0.4 cm. thick just over the tumor, 0.2 cm. in thickness at the upper end.

Stomach is contracted, particularly at the pyloric end; contains a small quantity of grumous material. Mucosa intensely hyperemic, at points almost necrotic. These changes most marked in the pyloric area. Summits of the rugae pointed and slightly eroded. Mucosa obscured by superimposed mucus.

Intestine: One hundred and eighty centimeters above the ileocecal valve is a bifid Meckel diverticulum. It is 6 cm. in length, arises from free margin of intestine, has a diameter of 1 cm.; 2 cm. from its origin it divides into two small sacs resembling the letter "Y." Its mucosa is normal, overlying serosa is somewhat thickened, otherwise intestine is normal. Large arterial trunks show considerable atheroma.

With the exception of a marked arterial sclerosis, there is no noteworthy lesion of other organs.

Histologic examination of properly prepared sections shows that the growth is a typical epidermoid cancer, a squamous-cell epithelioma with marked keratinization of the cell nests and a richly cellular stroma. A tumor possessing such a structure must be of very low order of malignancy, resembling in its architecture the least malignant of the labial epitheliomas.

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HYALINE BODIES IN TUMORS AND KINDRED OTHER CONDITIONS.*

BY

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The belief among a certain number of scientists at the present day of the infectivity of carcinomas and sarcomas, has led to quite an abundance of literature and study upon the subject. This belief has become stronger with some, as certain foreign bodies (supposedly coccidia and saccharomycetes) have been isolated by different observers.

In some experiments (Rabinowitsch's) granulation-tissue nodules were produced by inoculation of a few different varieties of torula. In other experiments (Sanfelice's) the same lesions have been produced by "yeasts" isolated from fruits. Gaylord in this country, has also observed an organism, probably a yeast, in certain tumors, which is said to have produced adenomas when inoculated into the lower animals. Loeb, in various experiments upon rats and mice, has proved beyond a doubt, that in one species, sarcomas can be produced by inoculation of masses of these growths. As yet he has not isolated any specific organism.

Roswell Park is a firm believer in the infectious nature of carcinoma, and cites a case of a man who had a pigmented mole upon his back which became irritated and ulcerated, and which eventually became malignant. This was followed by metastases occurring in the mediastinum, lungs, and heart. From the rapid course of this case, he seems justified in claiming that there is an infectious agent as a causative factor of the condition. Foulerton, Ruffer, Schüller, Busse, Ronelli, Plimmer, and others have seen, and in some cases, isolated "bodies" or yeasts from tumors and in other conditions.

The observations of Russell on what he calls "fuch-

* From the laboratories of the Jefferson Medical College Hospital.

sin bodies" in tumors, are very well known. The so-called "molluscum corpuscles" or "fuschin bodies," have been asserted by some to be coccidia, by others, yeasts or torulæ, and by still others as degenerated cells or nuclei. A hyaline, a mucous, and sometimes a colloid degeneration are spoken of as occurring in these bodies. The failure to cultivate them, irrespective of the methods tried, seems to speak against the microbic nature of the parasite (?).

The writer has also demonstrated certain bodies in malignant and benign tumors and kindred other conditions. These bodies are found in the "juice" of tumors, as well as deeply situated in the stroma, or among, and sometimes within, the cells of the tumor.

These bodies in the unstained condition are spheric, hyaline, nongranular, and refractile; some appeared to be encapsulated, but most of them were nonencapsulated. They are light yellow and yellowish-green, and unaffected when treated with ether, osmic acid, or Sudan iii. They closely resembled fat globules (for which the above named tests were made), but lacked the heavy outline of these globules. Sometimes one or more could be seen to be intracellular. They stained faintly in the fresh condition with eosin, and gentian violet. No budding was demonstrable. They did not change in shape when first observed, and the same slide examined several days later, showed the same picture just described, with no increase in the number of bodies.

At first glance the bodies appeared to be saccharomyces, but the absence of budding seemed very peculiar. The bodies did not contain granules or spores—peculiarities which *Saccharomyces cerevisiæ*, and few chromogenic yeasts possess. The size of the bodies varied from 5μ to 20μ in diameter; where numerous, they were small and averaged 5μ to 7μ , where few were seen, 10μ to 20μ was the usual size. In malignant growths these bodies have been observed with wonderful regularity, resembling the ones found in the fresh condition, and in a few instances, apparent buds were observed.

The method of examining sections was as follows: Small masses of the tumor were fixed in Heidenhain's solution of mercury bichlorid, dehydrated, and embedded in paraffin. Some were fixed in absolute alcohol and embedded in paraffin. Sections were then cut, and stained with 2% aqueous solution of gentian violet, followed by Gram's solution and decolorized with alcohol or anilin oil. Some of the sections were stained by the

ordinary method, with anilin gentian violet, followed by the usual technic. Others were stained by the Gram-Weigert method. Still other sections were stained with Unna's polychrome methylene-blue, followed by alcohol, while some were treated with styron. Carbol fuchsin, saffranin, and carbol toluidin-blue were also used. The stain was left upon the section from 15 minutes to 24 hours. When carbol fuchsin or saffranin was used, alcohol was applied until the excess of stain was removed. The specimen was then cleared with oil of origanum cretici or oil of cloves, and mounted in xylol balsam. Sanfelice's stain was used, but with unsatisfactory results. The sections were next examined with a $\frac{1}{2}$ -inch oil immersion, although with a $\frac{3}{4}$ -inch objective (Bausch and Lomb) the bodies could be seen. In superficial epitheliomas, in which ulceration had taken place, ordinary bacteria of suppuration were also present.

In the 57 malignant tumors examined, the bodies have been observed in all but one; some containing many, others only a few. They were more frequently seen in carcinomas than in sarcomas. These tumors include 23 cases of squamous-cell epitheliomas, 10 scirrhous carcinomas of the breast, 5 columnar-cell carcinomas of the intestine. One columnar-cell carcinoma of the stomach, 1 papillary carcinoma of the antrum, 3 scirrhous carcinomas of the liver, 1 encephaloid carcinoma of the breast, 1 carcinoma of the bladder (primary), and 6 columnar-cell carcinomas of the uterus. Three specimens of enlarged glands were also examined; two from cases of scirrhus of the breast, and the other from a case of columnar-cell carcinoma of the intestine. With the exception of 5 cases, the squamous-cell epitheliomas were taken from the margin of the upper or lower lip. The enlarged gland from the case of carcinoma of the colon, was made up entirely of cancer tissue.

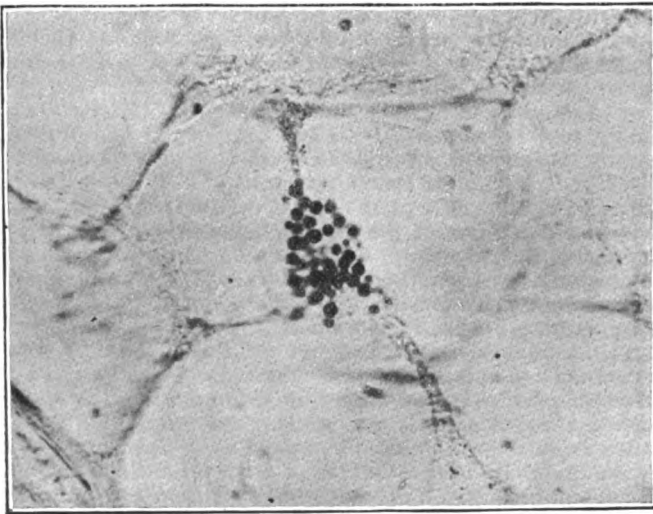
The sarcomas examined were a small round-cell sarcoma of the jaw, an angiosarcoma of the kidney, and an angiosarcoma of the breast. The bodies were found in the first two, but not in the last one.

Some sections contained only a few bodies. In each case they were deepseated; some appeared distinctly encapsulated, some were extracellular, and others intracellular. Where small and numerous, they were generally extracellular. Occasionally, one of these large bodies could be seen occupying the whole cell. Apparent budding was present in but 2 cases, in the angiosarcoma of the kidney and in the fibroid condition of the breast.

The bodies in the former were found principally in the large venous channels. Sometimes as many as 12 to 20 bodies were found in a group, and at other times only one or two could be found in a whole specimen. In the kidney they were suggestively encapsulated, and this appearance was especially noticeable where they occurred ungrouped.

In the small round-cell sarcoma of the jaw, the organisms were exceedingly few, only three or four being demonstrable in a number of sections studied.

They were also demonstrable in a case of intracanal-



icular fibroadenoma of the breast, scattered throughout the fibrous connective tissue and being nonencapsulated.

In a case in which a breast was removed for a probable malignant growth (but which upon histologic examination revealed a markedly fibroid condition with atrophy of the gland structure) the bodies were also found. Apparent budding was observed in this case.

A large number of bodies deeply seated in the connective tissue, extracellular and nonencapsulated, were demonstrable in a case of hypertrophy of the gums reported by Roe. They were also present in a case of

pharyngomycosis and in 4 hyperplastic tonsils, as well as in a mass of adenoids removed from the pharynx. In 2 cases of leprosy quite a number of the spheric bodies were observed in the skin.

The majority of the specimens were received either in Mueller's fluid, formalin or alcohol, so that inoculations could not be made; however, when obtained in the fresh condition inoculations were always made upon various culture media.

The media used were plain peptone agar, glycerin agar (6%), glucose agar (1%), acid agar, blood-smeared agar, milk, blood serum, plain and glycerin-smeared potato; in plain glycerin (6%) and glucose (1%) bouillon, upon bread paste, "næhrstoff" (von Heyden) with and without (6%) glycerin, and fluid from ascites. The fresh material itself was placed in sterile test-tubes and incubated.

The inoculations were made either from the "juice" of the tumor or from macerated tissue, or the tissue dropped directly into the culture medium. They were then placed in the incubator and also under anaerobic conditions. In cases in which the tissue was macerated and allowed to soak in bouillon, the bodies were demonstrable, but did not tend to increase in number. Inoculations were made in the peritoneal cavity of rabbits, of masses of tissue and macerated material from carcinomas, but in none of these did any reaction occur up to 18 months. The majority of the bodies found in the malignant growths here recorded, correspond morphologically to Russell's fuchsin bodies. The bodies took the acid dyes as well as the basic, and hence I believe, with some others, that these bodies represent degeneration of cells.

The appended table shows the number of specimens studied (74 in all), including tumors and various other conditions.

Nichols,¹ in 21 cases of alveolar cancers of various organs, was unable to find cancer bodies in 5 cases. In 14 epidermoid cancers, cancer bodies were seen in but 1 case; in 5 sarcomas, cancer bodies were never present. In an article upon cell inclusions and yeasts in malignant conditions, especially molluscum contagiosum, Nichols quotes the following literature:

Patterson² (1841) studied the secretion from cases of molluscum contagiosum, and was the first to mention the strange so-called molluscum corpuscles or bodies. He described these as a peculiar sort of nucleus.

Specimens.	No. of cases.	Bodies found.	Bodies not found.
Columnar-cell carcinoma of the uterus.....	6	6	
Epithelioma of lip.....	18	18	
Epithelioma of knee.....	1	1	
Epithelioma of labia majora.....	1	1	
Epithelioma of foreskin.....	1	1	
Epithelioma of esophagus.....	1	1	
Epithelioma of eyeball.....	1	1	
Scirrhus of breast.....	10	10	
Scirrhus of liver.....	3	3	
Papillary carcinoma of antrum.....	1	1	
Columnar-cell carcinoma intestine.....	5	1	
Columnar-cell carcinoma stomach.....	1	1	
Encephaloid of breast.....	1	1	
Carcinoma of bladder.....	1	1	
Papilloma of bladder.....	1	1	
Enlarged glands foll. carcinoma.....	3	3	
Angiosarcoma of kidney.....	1	1	
Angiosarcoma of breast.....	1		1
Small round-cell sarcoma of jaw.....	1	1	
Hypertrophy of the gums.....	1	1	
Hyperplastic tonsillitis.....	4	4	
Postnasal adenoids.....	3	3	
Pharyngomycosis.....	1	1	
Intracanalicular fibroadenoma breast.....	1	1	
Fibroid condition of the breast.....	1	1	
Chronic meningitis.....	1	1	
Leprous skin.....	2	2	
Molluscum contagiosum.....	1	1	
Hemorrhagic pancreatitis.....	1	1	

Von Baresprung³ (1848) spoke of these bodies as epidermic cells which had imbibed albuminous matter, and remarked that he had observed similar conditions in his investigation of sebaceous glands.

Virchow⁴ (1865) claimed that the newgrowth contained epithelial cells and nuclear bodies, arising from the hair follicles, and he described and likened them to swollen starch bodies. He spoke of them as fat-like globules surrounded by doubled contoured rims which resisted the action of water and acids, but became more translucent when subjected to the action of alcohol. He had observed the same bodies in epidermoid cancer and in the "follicles of the nail-bed," and said they resembled the porosperms found by Klebs in intestinal epithelium.

Bizzozero and Manfredi⁵ (1871) also observed these bodies, but do not state positively their nature and development; they assert that it is quite proper to affirm that they owe their origin to the protoplasm of the cells of the newgrowth. They noticed that the bodies were insoluble in hot ether, and in acetic acid.

Retzius⁶ (1871) believed that the bodies were *sui*

generis never associated with cancer or epidermoid growths, and did not arise from large epidermic cells, and that their size only (0.035 mm.-0.040 mm.) prevented him from considering them the spores of parasites.

Boeck⁷ (1875) found 2 forms of bodies: First, the so-called molluscum bodies which were round or oval, sharply bounded, transparent, nonnuclear, with a very doubtful double contour about them; second, strangely formed epidermic cells which were often without nuclei and which possessed sharply bounded outlines. From this second type Boeck asserted that the first arose and claimed that he had seen the bodies within the walls of the peculiar epidermic cells. Lukomsky⁸ (1875) stated his belief that the bodies arose from cells which had invaded the epidermis. O. Simon⁹ (1876) made the statement that the great size of the bodies spoke against the theory of parasites put forward by Klebs.

Kaposi¹⁰ (1877) also discouraged the theory that the molluscum bodies were parasites, because they never showed any signs of organic reproduction by proliferation or by budding. He also disputed their origin from the cell nuclei, for he asserted that one could often see the nucleus squeezed up against the wall of the cell. He did believe, however, that the peculiar bodies arose from the transformation of cell protoplasm and said that this could be demonstrated by following up the changes under the microscope.

Vidal¹¹ (1878) inferred from the jelly-like translucency of the bodies that they were the product of a colloid degeneration.

Renaut¹² (1880) claims that the bodies are a result of a hyaline change in the perinuclear zone of the rete cells.

Torok and Tommasoli¹³ (1890) demonstrated that the strongest acids and alkalies have little or no effect upon the so-called parasitic bodies. They believe that these bodies are a result of colloid degeneration. Stanziale¹⁴ (1890) states that these bodies react to caustic potash and to other chemicals not as parasites but as a substance akin to horny matter. Kuznitzky¹⁵ (1895) describes the molluscum corpuscles as homogeneously glossy, without the least granulation or sign of any nucleus. Benda¹⁶ (1895) states that he believes the bodies are epidermal cells with abnormal contents, which are always surrounded by a clear zone which is a vacuole in all probability. Unna¹⁷ (1896) believes that the bodies are only the results of colloid or hyaline degeneration of the

prickle cells; this differs from hyaline degeneration in carcinoma because it occurs in the interior of cells only. Audry¹⁸ (1899) states that the substance of the bodies is not homogeneous, but is composed of little blocks which, however, cannot be termed granular.

Busse¹⁹ in 1894 described cell inclusions which he had observed in the subperiosteal tissue of an albuminous periostitis of the tibia. The histology of the tissue showed young connective tissue, numerous giant cells between, and in which were numerous small circular refractile bodies with a double contour.

Inoculations made into different animals showed that these bodies multiplied; but Busse did not at that time claim that the bodies alone produced the lesions (gangrene, peritonitis, abscess) as ordinary pyogenic organisms were also present in the abscess. He cultivated the organisms upon ordinary media and because they produced carbonic acid he thought the organisms were probably yeasts. In another paper he gives the post-mortem findings in the case cited. In the pus from the bone lesions, in the pleura, in the lung, in the kidney abscess and in areas of the spleen, yeast cells were isolated. Inoculating pure cultures of these organisms into animals, nodules of suppuration at the point of inoculation were produced which subsided in a few months' time. White mice which were inoculated with the organisms died in a month's time with nodules at the site of inoculation, in the kidney, brain, lung and peritoneum. From all these lesions blastomycetes were obtained in pure culture. In the lesions the blastomycetes were generally surrounded by a gelatinous capsule which arose either from the yeast or from the tissues.

Following Busse's article, Sanfelice²⁰ published a paper in which he stated an inclination to believe that the wellknown cancer-cell inclusions were blastomycetes. He then obtained blastomycetes from fruits and inoculated animals. Guineapigs died in from 20 to 30 days with enlarged lymph-nodes, secondary nodules in the liver, kidney and spleen; from these lesions he obtained pure cultures of the organisms. In tissues studied he most commonly found them in the lymph sinuses. *Saccharomyces neoformans* was the name adopted by Sanfelice for this organism.

Sanfelice, in 1895, published an article setting forth that he had found in a primary cancer of the liver of an ox, small refractile bodies which histologically resembled his *Saccharomyces neoformans*. He obtained upon potato

and in media containing sugar, pure cultures of these bodies, which, when inoculated into guineapigs, caused death in 2 months, and produced nodules at the site of inoculation with enlarged lymph-glands. He found that the animals generally died within 30 days after inoculation into the testes, liver and abdomen. The organisms in the tissues showed a circular outline with double contoured membrane. Occasionally budding was observed and also hyphæ. In smears made from fresh tissue many leukocytes containing blastomycetes were observed.

He also obtained pure cultures of blastomycetes from human malignant tumors, from tumors of cattle and swine. This organism was not pathogenic for animals. After prolonged experiments he at last claimed that he had produced true cancer in a dog with blastomycetes. A bitch was used for the experiment and inoculations were made into the breast. Swelling resulted, but rapidly subsided. The animal died in about 10 months and the inguinal lymph-glands showed enlargement. The growth was an adenoma, but there were no metastases. There were a few blastomycetes found upon the periphery of the tumor, but none in the old part. Those found in the periphery were mostly free, but they did not correspond with the ordinary blastomycetes. This peculiarity Sanfelice claims to be due to the long time the organisms remained in the tissue, thus resembling the ordinary cancer inclusions, and in which stage it is incapable of culture upon ordinary media.

Plimmer²¹ claims to have isolated from human cancer an organism which grew anaerobically, and which corresponded morphologically with the cancer cell inclusions. Inoculations into some animals gave negative results, but in some the bodies could be demonstrated. Guineapigs which were inoculated intraperitoneally showed diffuse lesions in the omentum and internal organs. Upon histologic examination these nodules were seen to be composed of endothelial tissues which Plimmer calls tumors. He did not give to his organism any specific name.

Roncali²² observed cell inclusion in an adenocarcinoma of the ovary but was unable to isolate or cultivate these bodies.

Binaghi²³ demonstrated what he termed blastomycetes in 75% of epidermoid cancers. He claims that if given the entire tumor he would have had 100% positive results. His reason for calling the bodies blastomy-

cetes was that they corresponded in form, color and chemic reaction.

Mafucci and Sirles²⁴ found blastomycetes in peculiar nodules in the lungs of a guineapig. They were situated in epithelial cells of the nodules.

Again,²⁵ these 2 last-named observers cultivated blastomycetes from 6 out of 39 cases of cancers or sarcomas from men and animals. They decided that the living blastomycetes were in inflammatory cells while dead ones were in the protoplasm of epithelial cells, and that the blastomycetes represented an infection through an ulceration, because they never cultivated them from fresh aseptic living tumors.

Corsello and Frisco²⁶ claim to have obtained blastomycetes from human tumors, which when inoculated into animals produced neoplastic nodules with enlarged lymph-nodes. Leopold²⁷ cultivated blastomycetes from 4 out of 20 cases, which when inoculated into a white rat produced a very vascular giant-cell sarcoma with multiple metastases in the peritoneum. In both the primary and secondary nodules blastomycetes were found. Curtis²⁸ found blastomycetes in a nodule in the groin and back of a man, which were easily cultivated upon media to which sugar had been added. Inoculations into animals were generally negative as regards guineapigs and rabbits. In white rats a nodule of new formation usually occurred which would heal; or a general infection would result with metastases in the lungs and kidneys. Sometimes a nodule formed in dogs, which disappeared after a short time.

Gilchrist²⁹ isolated blastomycetes in a case of dermatitis; Rickett³⁰ observed blastomycetes in 12 cases of dermatitis.

Buschke³¹ isolated yeasts from ulcers of the skin and produced inflammation by inoculating them into the human subject. He also tried to obtain the organisms from cancers and sarcomas, but was unsuccessful. In endometritis, Colpe³² (in 1 case) claimed that it was due to blastomycetes; and Ernst³³ found yeasts in the urine of a diabetic patient.

Rabinowitsch,³⁴ in a very extensive series of experiments with 50 yeasts, found that only 7 were pathogenic for the lower animals, and in none of the inoculation experiments was there true tumor formation. Foulerton³⁵ was quite successful in producing nodules of granulation tissue in rabbits and guineapigs by inoculating with various blastomycetes. Richardson³⁶ examined 40

tumors bacteriologically, and from none of them did he succeed in isolating blastomycetes. Bonome³⁷ found yeasts in 6 out of 26 cancers, and also claims that the organisms occurred more often in tumors which were ulcerated and exposed. Sternberg,³⁸ in studying cancers found cell-inclusions which he claims are vacuoles, in which there are leukocytes or areas of mucous degeneration with contraction, giving rise to the appearance of areas of calcification or included red corpuscles.

In the cells of carcinomas, according to Ribbert,³⁹ observers have found in various stages of development coccidia (?) which were considered animated. The results of other observers, however, showed that these foreign bodies were degenerated cell and nuclear products, also epithelium and red blood-cells enclosed by leukocytes and lymphocytes. By homogeneous changes and by destruction large and small round bodies are produced which are enclosed in vacuoles occurring alone or grouped.

Hyaline bodies have also been observed in rhinoscleroma, syphilis, tuberculosis, cancer, malignant lymphoma, in the mucosa of the stomach and intestine; nasal polyps and lymph follicles.⁴⁰

CONCLUSIONS.

It is seen from the specimens studied that these bodies were observed with great regularity.

They were in most cases quite deeply situated in the tissues, while a great many more were seen intracellularly.

Some of them gave quite a typical reaction of amyloid material, while the greater number failed to give this reaction. Treating them with dilute hydrochloric acid failed to produce effervescence.

It seems to me that they correspond most closely to the fuchsin bodies described by Russell, and that they really represent some degenerative change occurring in the cell or cell nucleus. That they play some part in the etiology of the conditions in which they are found seems doubtful, notwithstanding the fact that they are found deeply situated and intracellular. They do not possess the peculiar intracellular characteristics which Plimmer's bodies do, being distinctly hyaline. They may, however, represent a hyaline or amyloid degeneration of blastomycetes.

The fact that cultures were not obtainable in any case

upon various media and the failure to demonstrate true budding seems almost positive proof that they are not blastomycetes.

I desire to express my thanks to Dr. W. J. Roe for the photomicrograph used in this article.

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ECTOPIA OF THE ADRENAL.

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THE object of this paper is to give a brief résumé of the cases on record and a short sketch of the histology and embryology of this gland so far as they bear upon ectopia of the organ.

Histologically, the adrenal is composed of cortex and medulla, the former consisting of zona glomerulosa, zona fasciculata, and zona reticularis. The capsule surrounding the organ is composed of elastica in the outer part and white fibrous connective tissue in the deeper portion. In the latter Joesten and Rauber found involuntary, non-striated muscle fibres. Besides these, bloodvessels, nerves, ganglia, accessory adrenals, and bands of cells of the zona glomerulosa are also found. The capsule does not strip and is thinner in children than in adults. In the outer part of the zona glomerulosa the cell groups are elongated, while in the lower part they are globular. These cell groups are surrounded by connective tissue and capillaries. The nuclei are large and the protoplasm of the peripheral cells less in amount than that of the deeper cells. Extra nuclei are sometimes found in these cells. This zone is quite irregular, and in children may even be wanting. The cells of the zona fasciculata are arranged in strands or columns between which are found the connective tissue, bloodvessels, and lymphatics. The cells are more regular and paler than those of the preceding zone and stain less readily. They contain, except in children, fat globules. The nuclei are smaller, granular, and situated in that part of the cell nearest the capillaries. There are usually, in these columns, two cells side by side. In the deeper layers

of this zone the cells are less sharply defined and the nuclei central. The zona reticularis consists of cells arranged in a network, the continuation of the columns of the zona fasciculata. The cells are small, nuclei large, and the protoplasm pigmented with a yellowish-brown substance. In old age this zone is irregular, and in places wanting.

The medulla is separated from the above by a layer of large, smooth cells. It contains a network of connective tissue bundles, within the meshes of which are fragmented chains or groups of cells which stain deeply with chromium compounds. The nuclei are large, and often there is but little protoplasm.

Nerves and ganglion cells are abundant. The vessels are numerous and large, especially the veins. The adrenals of the newborn and young children are rich in furrows. This is of importance in the formation of accessory adrenals. In youth and adult life they are smooth.

Reviewing briefly the embryology of the adrenal we find that it has a double origin. According to Hertwig,¹ Balfour, Braun, Kölliker, and Mitsukuri, the medulla is derived from ganglionic outgrowths of the sympathetic system. The cortex, however, has a greatly disputed origin. Balfour, Braun, and Mitsukuri hold that it is developed from mesodermic cells just anterior to the mesonephros in a concavity of the cardinal vein. Hertwig, Minot, Janosik, Weldon, Milhalkovics, Semon, Hoffman, and Hans Rabl consider it of epithelial origin. Janoski and Milhalkovics hold that it is developed from the head end of the genital ridge, or epithelial cells in that region, while Weldon, Hertwig, and Minot believe that it arises from the head end of the mesonephros. (See also Aichel.¹³) The cortex as it develops surrounds the medulla and finally almost completely encloses it.

According to Chiari² the adrenal is developed from the peritoneal cells at the head end of the sexual gland anlage. As it consists of the same tissue as the latter it remains in intimate relation with it until the development of bloodvessels and the permanent kidney breaks up this relationship. At or about this time small parts or collections of cells may become detached, such fragments or even the whole gland becoming ectopic structures.

In an embryo of the second or third month the adrenals lie in close proximity to the inferior vena cava. Later, with the descent of the

testis or ovary, small cell-groups or detached portions of the developing organ may be drawn away from their former positions and deposited at various places along the path of descent of the developing organs and especially through the necessary lengthening of the spermatic veins.

At this time the adrenals are comparatively large, enclosing nearly the whole kidney. The two are separated by connective tissue, the future capsule of the kidney. As the kidney is lobulated in the fetal condition it is easy to understand how small detachments of cells could be enclosed in the interlobular connective tissue at this stage, and so account for the presence of adrenal tissue in the columns of Bertini and other parts of the adult kidney.

Mention of accessory or misplaced adrenal occurs as early as 1568, followed by that of Morgagni, in 1740, and Duvernay, in 1751. Rokitsansky found bodies of various sizes in the region of or upon the normal adrenals, in the solar and renal plexuses, and even the cortex and medulla of the adrenal body itself. Klebs, in 1876, states that, in addition to the above places, accessory organs may be found upon the kidney, beneath the capsule, and even within the kidney substance itself. Since then such structures have been found in the region of the internal abdominal ring, in the inguinal canal, upon the spermatic cord, between the epididymis and testicle, in the broad ligament, and in structures neighboring to those mentioned. They have also been found in the liver and within the capsule of the adrenal.

Marchand,³ in his article of 1883, was the first to give a detailed description of these bodies. All his cases occurred in infants and children, and from this he drew the conclusion that in youth they disappeared and so were not met with in adult life. In his cases the bodies occurred in the broad ligament and in the region of the kidney.

In the first case the main body was found in the broad ligament, and smaller ones in the right adrenal. On section the larger one exhibited the cortex only.

The second, third, and fourth cases showed the accessory bodies in the broad ligament. The second one, on section, showed a yellowish-white edge and a yellowish-gray centre. It was, according to his conclusions, the only one to be found that exhibited anything like a true

medulla. Its cortical cells contained fat globules. The other two were practically the same as case one.

The fifth case exhibited a small body just behind the right kidney.

The sixth case showed a number of small ball-like masses on the kidney and to the median side of the adrenal. On section these showed only cortex.

The fallacy of Marchand's conclusion, that accessory adrenals were to be found in children only, was soon proven by the findings of Schmorl.⁴ His cases were adults, and he found a wider distribution of the accessory structures.

His first case, a man, aged thirty years, exhibited a small body just outside of the external abdominal ring. It lay upon the spermatic cord in close relation to the artery and the vein. It was yellowish-brown, smooth, pea-sized, and upon section showed a peripheral zone and a grayish-white centrum. In the latter the lumina of many small vessels were to be seen. The cortex showed adrenal substance, while the medulla consisted of delicate connective tissue and many bloodvessels.

D'Ajutolo⁵ found such a body on each spermatic cord, just within the internal ring, of a newborn infant. In Schmorl's second case he found a small mass 2.5 mm. by 1.5 mm. in the right lobe of the liver. This was sharply defined and consisted of a dark yellow periphery and a brownish, not well-defined centrum. The cortical cells were in groups surrounded by delicate connective tissue and thin-walled bloodvessels. The zona fasciculata showed fat globules and in some cells yellow pigment. In a woman, aged thirty years, he found three small bodies in the liver, and in another case two in the right lobe. In his next case the accessory adrenal structure occurred (in the liver) as a well-defined mass, about the size of a hazelnut. The cell protoplasm was pigmented, while some of the columns of cells showed hyaline degeneration. The centrum contained many bloodvessels.

The liver, no doubt, makes an effort to dispose of these foreign cells, and in some cases is successful, while in others the cells persist, multiply, become encapsulated and produce masses such as that just mentioned. (See also Noyes.¹¹)

Schmorl demonstrated a wide distribution of ectopic adrenals and also that such malposition occurred in adults, both male and female.

Chiari,² in 1884, reported several cases. In his first case a small body was found posterior to the right kidney. It was about the size of a pea, yellowish-brown in color, and on section showed only cortex. The centrum consisted of bloodvessels and delicate connective tissue, and just external to these structures pigment cells were noted. Beyond this was the rest of the cortex. All three zones were distinct and all contained fat, the zona glomerulosa being richest in this element.

The second occurred in the broad ligament of a woman. Here the pigment zone was well marked, and the centrum especially so. The cells of the zona reticularis were pigmented and the whole mass encapsulated.

The third showed a small mass beneath the right kidney, near the adrenal, and the fourth also beneath the right kidney. Here the general characteristics were the same.

Ulrich⁶ reported an adrenal in the kidney, another upon the upper pole of the right kidney, separated from the renal tissues by the capsule of the kidney. The same observer noted two other instances, both in children, one fourteen days and the other three years old. His third case showed all three zones, no medulla, no fat, and no pigment.

Dagonet's⁷ first case showed a pea-sized body in the broad ligament just below the ovary. In the second there were two, one lying between the testicle and epididymis, and another on the spermatic cord. Of these the first showed the zona glomerulosa and zona fasciculata and a centrum rich in capillary bloodvessels. The cell stained deeply, but contained neither fat nor pigment. He made the observation that in children the centrum was red and the vessels filled with blood, while in the adult the centrum was usually pigmented and dark.

Kelly⁸ reported a case in which there was union of the adrenal and kidney and a displaced mass of the former, irregular in shape, in the cortex of the latter. The little adrenal islets had portions of kidney cortex enclosed within them. Besides these, there are the cases of Rossa (quoted by Warthin¹⁸), four in the broad ligament, and of these two in newborn children; those of Meyer, seven in children and fetuses; and Gottschalk's, one in an adult. Wahneau reported a case in which an ectopic adrenal was found in the celiac ganglion.

The occurrence of ectopic adrenals is not so infrequent as might be supposed. Imbert⁹ states that they occur in about 92 per cent. of all

autopsies, and they are found in the kidney in 6 per cent. to 8 per cent. of cases. Eastwood¹⁰ calls attention to the malignancy of the neoplasms, developing from adrenal rests. His paper takes up those occurring in the pelvis in connection with the spermatic and ovarian veins and broad ligament. He found a large malignant tumor in the fundus uteri. It consisted of a large, encapsulated mass the cells of which resembled those of the zona glomerulosa. Imbert⁹ experimented on dogs with the view of producing tumors composed of adrenal tissue. He detached the left adrenal and inserted it into a longitudinal incision in the kidney, and studied the results in the animals that recovered. In one dog three and a half months after operation the tumor resembled the so-called pseudolipoma of the kidney. He considers this an experimental pseudolipoma of the kidney. In another case he produced a cystic condition.

The importance of ectopic adrenals is not their frequency, but the frequency with which they give rise to neoplasms. Their importance is being more fully realized as tumors supposed to be lipomas and adenomas are found to consist, histologically, of adrenal rests.

Grawitz¹¹ first directed attention to the fact that certain tumors of the kidney were composed of adrenal tissue, adrenal rests, and Kelly⁸ in an exhaustive review of hypernephromas has fully summed up the various views as to their origin and general character.

Ectopic adrenals respond to the following tests:

1. *Histological.* The peculiar, indeed, quite characteristic architecture of the organ as a whole as well as its component layers.

2. *Chemical.* Gives the reaction for glycogen. The specific brown coloration in chromium fixed preparations, said by Böhm and Davidoff not to be observed elsewhere except in certain cells of the hypophysis.

3. Presence of fat globules in the cells, especially in the zona glomerulosa.

4. *Staining reaction.* By the use of Weigert's fibrin and Russel-fuchsin stains, Lubarsch¹² found that the nucleus and nucleolus of adrenal cells stain differently. No other tissue responds to this test.

After this brief résumé of the occurrence of accessory adrenals and the histology and embryology of the normal gland, I desire to report the following case:

The patient,* J. L., male, aged twenty-nine years, was admitted to the Jefferson Medical College Hospital, the diagnosis being gumma or tumor of the brain; although the previous history yielded no satisfactory data, it was believed that the lesion was syphilitic. Had recurring convulsions that at the time of admission were uncontrolled by usual remedies, and occurred every fifteen minutes. He was trephined for the purpose of reducing pressure and as an exploratory procedure. Death occurred on the following day.

Autopsy by Prof. Coplin, to whom the writer is indebted for the use of the autopsy record, the material, and suggestions in the preparation of this report.

Pathological Diagnosis: Numerous hemorrhages in subcutaneous fat, spleen, and subserous tissues; cloudy swelling in the heart, liver, and kidneys. Hypostatic congestion and pulmonary oedema; lobular atelectasis. Ectopic of adrenal; intense meningeal congestion; gumma in left frontal lobe.

Only so far as bearing upon the matter at hand, will it be necessary to give a summary of the autopsy notes.

The kidneys were about normal in size, but somewhat flabby. Internally they showed but little abnormality. Upon the anterior superior surfaces of both kidneys a thin yellowish body was noticed. This covered an irregular area about 3 cm. in diameter, and approximately 1 mm. thick. The peripheral portion was yellowish, while that toward the cortex of the kidney was dark. They were beneath the capsule in each instance, and in places dipped into the cortex. One adrenal of normal shape, size, and location was present on the right side.

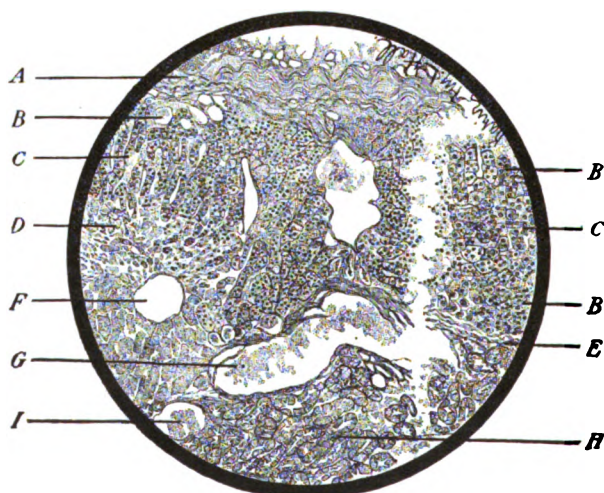
Upon the under surface of the liver near the transverse fissure, a small, thin mass was noticed. It resembled that upon the kidney. It was approximately 1 cm. in diameter and 0.2 cm. thick, tapering at the ends like a small adrenal. Upon section it had the appearance of normal adrenal tissue. Pieces of these masses were placed in Heidenhain's solution and Müller's fluid, dehydrated in ascending strengths of alcohol, cleared in turpentine, and embedded in paraffin.

Adrenal in the kidney. (See Fig. 1.) Upon histological examination the adrenal, in connection with the kidney, showed the following structure: The capsule was rather thick and composed of white fibrous connective tissue. In the deeper layers were apparently some involuntary non-striated muscle fibres. Between the groups of cells of the zona glomerulosa and capsule were many red blood cells. These were also noticed scattered between the glomeruli. The groups of cells of this zone were large and small; in places these were wanting, the zona fasciculata

* For this brief abstract of the history the writer is indebted to Dr. Spencer. Other features of the case will be reported elsewhere.

reaching nearly to the capsule. In others the glomerular zone was five or six groups deep. The edge of this patch of adrenal tissue tapered, and at the extreme margin the capsule was seen separating it from the kidney cortex, but for only a short distance. Here the zona glomerulosa followed the capsule to its end. Over this area the regular capsule was quite thick and apparently laminated. Between the lower layers were extensive but narrow spaces containing large

FIG. 1.



Section of cortex of kidney containing ectopic adrenal. (Fixed in Heidenhain's solution, paraffin, hæmatoxylin, and Van Gieson. Obj. 16 mm., oc. compensation, and reduced $\frac{1}{3}$.) A. Capsule of kidney extending over adrenal B B B. Zona glomerulosa. C C. Zona fasciculata. D. Zona reticularis. E. Capsule projected between adrenal and kidney cortex partly separating the two structures. F. Cavity surrounded by Bowman's capsule, external to which is adrenal tissue. G. Large vein. H. Kidney cortex. I. Imperfectly developed Malpighian body.

numbers of red blood cells. Beyond the area of true adrenal tissue this capsule extended as a thick mass of connective tissue in which were great numbers of erythrocytes. Here also were found fat and elastic tissue, the latter continued from over the area of adrenal substance. Within the capsule were also groups of cells resembling those of the zona glomerulosa and separate cells, which took the nuclear stain quite deeply. These latter cells were arranged in a band in the middle

of the capsule, and as the adrenal substance was reached the band became broader and ended abruptly.

At one place a beam of tissue, apparently involuntary non-striated muscle fibre at its inner end, passed in at an acute angle, cutting off a triangular portion of the adrenal cortex. Large and small bloodvessels were present in abundance and nearly all filled with blood cells.

Just beneath the capsule was a single row of cells that extended quite a distance. They appeared the same as the rest of the cells of the zona glomerulosa. Beneath this the groups were large and irregular. The number varied from two to six in depth. The cells and nuclei of those nearer the capsule were small, with outlines usually indistinct. Most of the remaining nuclei, however, were large and prominent and took all stains deeply. They were circular in outline and mostly eccentrically placed. The nuclear membrane was sharply outlined, and in those cells less deeply stained the nuclear fibrils were seen in various arrangements, apparently karyokinetic figures. The nuclei varied from six to thirteen microns in diameter, the average being about eight to nine. The cell protoplasm stained but faintly and irregularly, giving the appearance of fat globules. The outlines were usually indistinct, and the diameter varied from eighteen to thirty microns. A few had two or three nuclei. Between the groups, beneath the capsule, were noticed red blood cells scattered and grouped.

Zona fasciculata. The columns were long and parallel as in the normal structure, and separated by connective tissue. The cells were larger than those of the zona glomerulosa, and the nuclei averaged ten to twelve microns in diameter. These were placed eccentrically toward the centre of the columns and showed karyokinetic figures. The protoplasm stained more deeply and more regularly than in the above zone, and the cell outline was also more distinct. The cells in the lower portion of this zone were of a peculiar olive-green color, the nuclei deeply stained, and the whole somewhat hazy.

Zona reticularis. Here the cells were smaller and the nuclei comparatively large, averaging ten microns. Frequently two were seen in a single cell. The nuclei were irregularly placed; no matter what stain was used the cells were of a peculiar olive-green color and somewhat hazy. They were indiscriminately scattered and not arranged in definite chains, groups, or network. The cell outlines were more distinct than in the other zone. Some of the nuclei were quite distinct, showing peculiarities of those of the other zones. Here also a great many red blood cells were noticed scattered and in groups. A number of tubules, about eleven, were noticed here. These were lined by simple squamous epithelial cells and two contained imperfect Malpighian bodies. This zone passed directly into the cortex of the kidney,

except at the outer edges of the patch. At this portion the zona reticularis was absent. Between this zone and the cortex at places larger spaces were visible, apparently cystic in character, perhaps greatly distended capsules of Bowman, as they were lined by simple squamous epithelial cells.

Mass under the liver. (See Fig. 2.) Here apparently the order of the zones was reversed. Separating this mass from the liver was a thick layer of loosely arranged connective tissue containing oval

FIG. 2.



Section of ectopic adrenal beneath the peritoneum and intimately attached to the capsule of the liver. *AA.* Capsule of Glisson. *BB.* Zona glomerulosa. *CC.* Zona fasciculata. *DD.* Zona reticularis. *EE.* Peritoneal surface.

masses of cells apparently adrenal glomeruli, pigmented as those of the zona reticularis.

The zona glomerulosa was only two or three cell groups in depth. The cells were smaller than those in the foregoing specimen and stained more deeply. The nuclei averaged nine to ten microns, were eccentrically placed, and stained intensely. Blood cells were found between the groups. In the zona fasciculata the cells were also smaller than those in the kidney, but the nuclei were larger. The latter averaged twelve to fourteen microns, were eccentrically placed, and stained deeply. The cells were darker than those of the third zone. The

columns were quite long and well separated in places. The zona reticularis stained well, the nuclei were prominent, and the cell protoplasm was less hazy than in the kidney specimen. The cells were as large as those in the zona reticularis of the above, but deeper in color, containing, apparently, more pigment. The network was closely meshed, especially in the deepest part, where the cells formed an almost solid mass the extent of the section. Here the color was an olive-green.

Over the greater extent of this mass was a band of tissue, apparently representing the peritoneum. In places the strands of this tissue were separated, and the spaces contained an abundance of red blood cells. For quite a distance it gave way to several layers of large polygonal epithelial cells. The nuclei were prominent and eccentrically placed, but the cell walls were indistinct. The cells were deeply colored, like those of the zona reticularis, but separated from them by connective tissue and bloodvessels in places.

From the above it will be seen that the zona reticularis was external, a very unusual condition.

CONCLUSIONS. 1. Ectopic adrenals are found in both sexes and all ages. 2. Their occurrence is far more frequent than formerly supposed. 3. Although they vary in size, most of them conform to the general description of yellowish, oval, or globular bodies, which on section show a light periphery and a dark centrum. 4. Microscopically these bodies consist of two or three zones of the cortex of the adrenal, but seldom of the medulla. (Marchand's second case was the only exception, and no complete histological description was given.) May,¹⁶ however, found both cortex and medulla in two out of ten of his cases. 5. The separation of the masses occurs early, before the inclusion of the medulla by the cortex of the normal gland. 6. The distribution varies greatly, the usual location being some point between the kidney and the descended sexual gland; to this is to be added the unusual location, the under surface of the liver, and also within the organ.

NOTE.—While this paper has been in the hands of the printer, Joseph C. Ohlmacher (*Journal of Medical Research*, May, 1902, vol. vii. No. 4, p. 421) has reported a malignant medullary hypernephroma of the kidney.

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**CYSTIC DEGENERATION OF THE MAMMA SHOW-
ING TRANSFORMATION INTO SCIRRHOUS
CARCINOMA.¹**

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(From the Laboratories of the Jefferson Medical College Hospital.)

THE microscopic specimen that forms the basis of this communication was obtained during the study of a mamma removed from a woman of sixty-three years by Dr. W. W. Keen, through whose courtesy I am permitted to report the findings. The mamma contained a hard nodule 2.5 centimetres in diameter to one border of which was attached a long, thin band of tissue having the same general characteristics as the nodule itself. A number of the axillary lymph nodes were enlarged and hard. Histologic examination shows that portions of the mammary gland are involved by chronic interstitial mastitis, as evidenced by the presence of an increased amount of perilobular and intralobular connective tissue. This change, however, is not a conspicuous feature of the specimen. Many of the lobules are the seat of cystic degeneration, or involution, that has transformed them, in some instances, into a single cavity lined by one or more layers of low cuboidal or polyhedral epithelial cells. In other instances, several small

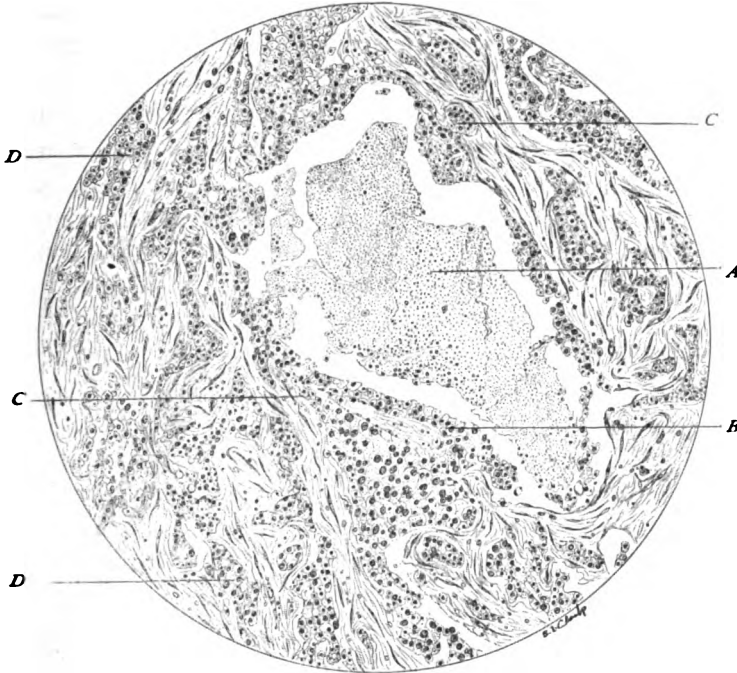
¹Read before the Pathological Society of Philadelphia, May 28, 1903.

cavities are found in a lobule, distinct evidence of beginning coalescence of some of them being present. Many of these cavities are partially filled by masses of granular *débris* containing epithelial cells exhibiting varying degrees of necrosis. The most important departure from the normal, shown in certain of the sections, is the presence within the stroma of irregularly outlined masses of polyhedral epithelial cells. These cells are not limited by any *membrana propria*, but infiltrate the tissue in an irregular manner (Fig. 1). A significant fact is that, at several points in the wall of one of the large cavities previously described, the epithelial cells forming the lining have broken through the wall and are directly continuous with the irregular masses of cells contained in the adjacent fibrous stroma. This cavity contains a large amount of granular *débris* and partially necrotic cells, and in other ways shows its identity in type with the cavities that are bounded by a *membrana propria*, and have been formed, or are in process of formation, from the acini of the gland. The enlarged axillary lymph nodes contain large masses of epithelial cells similar to those in the mamma.

The diagnosis rendered in this case—cystic involution of the mamma undergoing transformation into a scirrhus carcinoma—brings up a question that has been debated at length, many surgeons not believing that this change occurs. The study of a number of specimens of both cystic involution and carcinoma of the mamma has led the writer to believe that there is an intimate relationship between the two conditions. In other words, cystic involution may be, and perhaps often is, followed by carcinomatous change. It being impossible to prove this by the microscope in many instances, the present specimen, showing direct extension into the surrounding tissue of the epithelium lining a cyst, is thought to be worthy of exhibition.

Gross,¹ when considering the development of carcinoma, pictures much the same condition, but speaks only of the enlargement of acini or ducts, with proliferation and final exten-

FIG. 1.



Carcinoma arising in a mamma the seat of cystic disease.

A. Necrotic detritus contained within a cyst.

B. Proliferating epithelium lining the cyst. At points this layer shows desquamation into the cyst cavity.

C. C. Two points where the epithelial lining of the cyst is continuous with the epithelium of the alveoli of adjacent carcinomatous tissue.

D. D. Epithelial nests characteristic of this type of carcinoma.

sion of their epithelium, without mentioning previous cyst formation. That he did not consider cystic change to be a preliminary step in cancer formation is shown by the state-

ment made in the chapter on cysts,² where he says, "In either event, the prognosis is favorable, as it is in all the cystic formations of the mamma."

Snow,³ under the title of "The Malignant Reversion of Mammary 'Cystic Fibroma,'" reports two cases,—one of transformation into carcinoma, the other into sarcoma. By cystic fibromas, Snow means the cyst formation that accompanies connective-tissue hyperplasia during the period of devolution or degeneration of the female breast after the approximate age of thirty-four years. This we take to be the origin of the cysts in the specimen under study. He states that the condition increases slowly for a term of years as a benign tumor, but surely in the end becomes associated with malignancy, either carcinoma or sarcoma, the former originating in the epithelium lining the cysts, the latter in the surrounding fibrous walls.

Sheild⁴ does not speak directly of the relation of cysts to carcinoma, but, after referring to the almost invariable presence of cysts in chronic mastitis, says that "The transition from chronic mastitis into cancer is considered so common as to have received notice from every writer on surgical pathology." For his own part he is inclined to the belief that many cases of cancer supposed to supervene upon chronic mastitis were cancer from the beginning, and that no previous chronic inflammation existed. Like Gross, he states that an early cancerous change is doubtless the spread of proliferating acinous epithelial cells into the connective tissue, but he does not mention cysts. He expresses serious doubt as to the generally accepted belief in the connection between cancer and chronic inflammation of the breast substance itself. The same writer in a later article⁵ advocates as treatment of cystic disease removal of the cysts or the injection method instead of amputation of the breast.

Johnson⁶ cites the case of a woman who had the left breast excised, because of cystic degeneration, in 1877. In 1882, the right breast was excised on account of the presence of a like condition. In 1889, a tumor which had been slowly growing for two years was removed from above the middle of the scar in the left side. This was found to be made up of two cysts containing papillary growths. The cysts were supposed to have developed from a fragment of mammary tissue left at the first operation. The chief interest in the case, according to Johnson, is found in the recurrence after ten years. This recurrence, especially of the type of cyst described, is to me suggestive of malignant disease.

Robinson⁷ reports a case of diffuse cystic degeneration of both breasts, the right being amputated in August, the left in November, 1894. The right showed chronic interstitial mastitis, was riddled with cysts, and contained evidence of carcinomatous change. The left was similar, with the exception that no malignant transformation was noted. Robinson believes that there is a causal relation between cyst formation and malignant growth, and that cystic disease of the mamma should be subjected to radical treatment.

Bull⁸ begins the treatment of cysts of the breast by aspiration. Later operation in cases that refill, etc., is confined to excision of the cyst only. He states that there is little evidence that this condition degenerates into cancer. If it does, cancer certainly may be slow in its development. Cysts developing at or near the time of the menopause need not be interfered with.

Bryant,⁹ who at first argues against the causal relation of cystic disease and cancer, later drops this argument, and confines his discussion to the comparative merits of conservative and radical operations for cystic degeneration. His statements are somewhat conflicting. He says there is no reason to believe

that women who have these cysts are more prone to cancer than those who do not have them, and that the condition is mostly amenable to local treatment without sacrifice of the breast. Later he states that "it seems probable, however, that all large cysts of the breast, if left untreated, will sooner or later become the seat of some proliferating intracystic growth which will be papillomatous, sarcomatous, or carcinomatous in its nature, according to the proclivity of the tissue to form, or of the individual to develop, either special variety." Bryant is an advocate of early operation for breast disease, for the following reasons: "Delay in removing the local disease, whether cystic or solid, is fraught with danger, whereas by early interference nothing but good can be achieved. In my belief, the presence of a simple cyst in the breast is no harbinger to future evil if it be treated and removed, although if left it may, without doubt, become a source of mischief; should a cyst containing intracystic growths be left untreated, it to a certainty will develop into a serious local affection." The treatment advised is the swabbing of simple cysts with carbolic acid or zinc solution and the removal of cysts which contain any intracystic growth. We take from Bryant's article that he admits the possibility of cystic disease becoming malignant, but his principal argument is nevertheless for conservative treatment of the condition.

Jonathan Hutchinson¹⁰ says: "It is admitted that these cysts start in the terminal acini or ducts, and are due to the constriction of the wall by the increasing fibrous tissue. The changes that the lining epithelium undergoes readily suggest a termination in cancer, but I believe with Bull and others that there is no proof of such transformation. The matter is of practical importance; many such breasts are excised with the fear that cancer will supervene; but there is an important

argument against such excision, namely, that when one breast has become the seat of fibrous degeneration and cyst formation, the other gland will probably follow suit. Few women would submit to the successive removal of both breasts unless there was really good reason for believing that grave danger was thereby avoided. I would repeat that there is no evidence that carcinoma especially selects the breasts that are the seat of multiple cysts, and that, unless the patient is very anxious about the condition, it is better to leave them alone."

The question of treatment is beyond the province of this paper; the foregoing references to the literature of the subject being given because of their bearing on the pathological problem under consideration. It will be noted that exceedingly diverse opinions are held.

In only one way can these differences be reconciled and the true relation of the two conditions determined, and that is by the co-operation of the surgeon and pathologist, the former observing critically the clinical history of these cases, *whether operated on or not*, the latter making a careful and complete histological study of removed specimens. The question is not one for mere theorizing or the occasional exchange of conflicting opinions. Its settlement means much. Negative proof of the change means to a certain number of women the saving of one or both breasts; positive proof means to a larger number of women the saving of life. The cause of cancer is unknown, and the results of treatment are in too many instances disheartening. The only hope of lowered mortality at present offered by surgeons is that of earlier diagnosis and operation. Operation during the precancerous stage of certain affections known at times to undergo malignant change, as leucoplacia linguæ and gastric ulcer, has its advocates. It is high time for the surgeon and pathologist to determine more definitely whether

cystic degeneration of the breast is a precancerous manifestation. This is simply a question of earlier diagnosis, a problem to which every surgeon is committed.

In closing, the writer wishes again to emphasize his belief in the strong probability of malignant transformation occurring in cases of cystic degeneration of the female breast. The accompanying specimen, showing the transformation clearly, is offered as a contribution to the evidence in favor of the view indicated.

[NOTE.—Since this article was put in the hands of the printer, there has appeared a valuable contribution to the study of cystic disease of the mamma by Greenough and Hartwell.¹¹ They have examined a series of thirty cases of this condition, which they prefer to designate as chronic cystic mastitis, following the suggestion of Koenig. In three of the thirty specimens carcinoma was present as a secondary lesion, but was of the adenocarcinomatous type, no evidence of scirrhus being found. The writers conclude that "the danger of the transition of chronic cystic mastitis to adenocarcinoma is sufficient to make the removal of the entire gland advisable in all but very early and slight degrees of the affection." The operation advised is the subcutaneous resection of the entire gland without removal of the nipple.]

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SECONDARY CARCINOMA OF THE LUNG (HEMATOGENOUS INFECTION).

BY W. M. L. COPLIN, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

I am indebted to Dr. E. Q. Thornton for the privilege of making an autopsy in this case.

The patient had had scirrhus cancer of the right mamma for at least two years. She had persistently refused operation, and had resorted to numerous quacks without any material alteration in the tumor. There had been but little ulceration, and clinically the tumor was apparently of the type commonly designated atrophic or withering scirrhus. The axillary glandular enlargement was not conspicuous. We were permitted only to examine the thoracic and abdominal cavities; the central nervous system was not examined.

The viscera generally were not macroscopically involved, with the exception of the lungs and a few small nodes in the liver. Neither macroscopically nor microscopically were the other organs cancerous. The pericardium was not cancerous.

The most interest in the case is in the pleura and lungs. The lungs did not recede when the chest was opened. They were a little more dense than usual, but nowhere were they solid or airless. The groundwork of the lung was a little darker in color than the normal lung. There was no edema and no marked con-

gestion. A conspicuous feature both on the pleura and incised surfaces was the presence of grayish nodules varying in size from scarcely perceptible pin-point, dot-like areas to masses 0.5 cm. in diameter. These latter nodules are upon the pleura. They are grayish or pearly white, rising above the pleural surface to a height of 4 mm. or 5 mm. The smaller areas are not elevated, but can be seen through the pleura. The organ is incised with possibly a little more resistance than normal; its cut surface is universally and quite uniformly dotted over with grayish markings similar to those noted as present upon the pleura. The resemblance of these bodies to miliary tubercles is quite striking. None of them show any caseation. At a few points along the interlobular septa there are grayish streaks indicative of linear distribution of a lesion similar to that presented in the nodular areas. There is no evidence of infarction. The lung is not edematous; the pleural cavity had been obliterated by adhesions and the lobes of the organs fused.

We were not permitted to dissect up the axillary vessels, so it is quite impossible to say exactly how the original neoplasm had reached the blood supply.

Histology. The air vesicles are free from any exudate; the larger part of the lung structure presents no important alteration. The conspicuous figures are quite characteristic cancer areas rather of the scirrhous type, neither the cancer cells nor the stroma showing any unusual feature. The carcinomatous infiltration of the organ occupies nearly all anatomic areas. It is inter- and intralobular in the vesicular walls, around the bronchi, along the course of the septa, immediately beneath the pleura, etc.

The second interesting point is the presence within the blood-vessels of numerous cancer emboli. Only occasionally one finds a small vessel actually plugged by cancer; for the most part the cancer cells are found lying free in the blood, and sometimes in one vessel of some size clusters of cancer cells can be recognized. They possess the same tinctorial and morphologic characteristics

as the cancer cells recognizable in the lung tissue, and are quite like the cells seen in the original growth. The unusually wide distribution of this process in both lungs and the presence of emboli in the blood clearly establish the hematogenous dissemination of the lesion.

December 12, 1901.

ABSCESS (CHRONIC) OF LIVER, RECRUDESCENCE DUE
TO SECONDARY INFECTION(?); THROMBOSIS
OF HEPATIC VEIN AND VENA CAVA;
EXTENSIVE NECROSIS OF LIVER;
HEMORRHAGIC INFARCTION(?).

BY W. M. L. COPLIN, M.D.,

AND

L. H. PRINCE, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

Anatomic Diagnosis. Chronic adhesive peritonitis; purulent peritonitis; chronic abscess of liver; thrombosis of vena cava; acute nephritis. (Only the liver presented).

M. R., aged fifty years; nativity, Italy; occupation, laborer.

On inspection *in situ* the organ extends 3 cm. below the costal arch, and appears to be slightly enlarged. The organ is lightly adherent to the diaphragm. When these bands are broken down a number of pockets of purulent fluid are disclosed. This fluid was identical in appearance with that found in the peritoneum—*i. e.*, a thick and grayish-colored fluid, in which were varying sized flocculi, of a yellow, somewhat dense material—the abdominal cavity contained 3500 c.c. of this fluid; specific gravity, 1020. On inspection, after removal, a large, slightly elevated, pale area is located on the posterior part of the upper surface. This area is entirely on the right side of the suspensory ligament, and is 10 cm.

in diameter. It fluctuates upon palpation. On incision this is found to be a cavity 15 cm. in diameter, containing 300 c.c. of a viscid, pale yellow fluid, which, after standing about thirty minutes, congealed so that inversion of the vessel without loss of contents is possible.

After careful cleansing the wall is seen to be quite ragged on its inner surface, of a lemon color, somewhat translucent in appearance, and varying from 0.5 cm. to 1.5 cm. thick. The parenchyma of the liver is brownish in color, with a network of yellow traced over the cut surface. The lines of the mesh range from 0.5 mm. to 1 mm. wide over the larger part of the surface; but as the abscess is approached these lines widen and blend with the substance of the wall and partake of the color of the wall.

On severing the hepatic vein a thrombus is incised. This thrombus is found to be continuous with one in the vena cava (inferior), extending from the right auricle to the saphenous and femoral veins of the left extremity. The right branches of the common iliac are less involved. An extensive edema of the left leg was noted.

Section of the radicles of the hepatic vein discloses the presence of a thrombus along these structures, and in a few instances the thrombus reaches the smaller branches. The organ weighs 2100 grams. Specimens were fixed in Beasley's fluid, infiltrated in paraffin, sectioned, and the sections stained in many ways. The pus was examined, stained and unstained; cover-glass spreads and inoculations on various media were also made.

Sections including the wall of the abscess and the adhering contents of the cavity show this contained material to be composed mostly of polynuclear cells, a large amount of cellular detritus, and free and fragmented nuclei. This cellular aggregation and necrotic material is surrounded by a zone of young granulating tissue, in which elastic tissue is quite abundant. All the elements usually found in this type of tissue are readily recognized. This zone fades into a layer of rather dense, wavy, fibrous

tissue, rather rich in spindle cells, among which are somewhat circumscribed polynuclear and lymphoid cell accumulations. This zone averages 1 cm. in width. An area of much altered liver structure is now observed surrounding this band of fibrous tissue. The cells of the organ are in an advanced state of necrosis. The outline of the cells is obscure, in many instances even lost, and where any cell resemblance remains the protoplasm of these cells is exceedingly granular. The nuclei present a peculiar granular appearance that is very striking. The areas of necrosis for the most part are located in the so-called arterial or intermediate zone of the lobules, and where the degeneration is most marked the polynuclear cells are conspicuously abundant. A rather large number of double nucleated cells tinctorially resembling liver elements are observed. The least affected of the liver structure is seen to be distributed in small islands around the lesser bile ducts and hepatic central vein, and is seldom more than three to four cells wide. The portal vessels are conspicuous and surrounded by irregular bands of fibrous tissue. These areas are notably infiltrated with lymphoid and a very few polynuclear cells. The columnar cells of the bile ducts are faintly granular.

A study of one of the smaller veins shows a thrombus of fibrinocellular tissue. The wall of the vein containing this thrombus is thickened, extensively fibrous, and contains a large amount of elastic tissue. Organization of the clot is well shown at its periphery, where can be seen the presence of fibrous tissue in rather prominent outline, quite well infiltrated with spindle cells. Other vessels show a remarkable proliferation of the endothelium that extends in plates into the lumen.

The periportal distribution of the liver tissue is quite conspicuous in the sections somewhat removed from the abscess area. The number of layers of cells around the ducts and vesicles is somewhat larger than in sections nearer the abscess.

The necrosis is more readily recognized as being of the coagulation variety, and shows an abundant infiltration with blood cells.

Other sections show the necrosis to extend from the central vein of the lobule. In the necrotic areas the liver cells are destroyed completely, there remaining only threads of connective tissue, forming meshes, which meshes are packed with well-preserved erythrocytes. The central veins do not appear to be at all dilated. It might be said that some of the areas in this part of the specimen appear, at first glance, not unlike the caseous areas of chronic tuberculosis. A coppery-brown granular pigment is observed in some of the liver cells.

A careful search in the pus and abscess wall failed to disclose the presence of any body resembling an ameba.

Bacteriology. The spreads contained an encapsulated diplococcus and a slender bacillus. By plating, cultures of the staphylococcus pyogenes albus and colon bacillus were obtained; the encapsulated coccus, arranged in pairs, and by far the most conspicuous organism in the spreads, was not cultivated. The diplococcus presents the morphology and tinctorial characters of the pneumococcus.

Diagnosis and Remarks. This patient had lived in districts where amebic dysentery occurs, but no history of the affection could be obtained. The intestine was entirely free from lesions. The wall of the abscess clearly indicates that it is old, possessing a fully developed fibrous layer limiting the cavity, and with progressing fibrosis extending at its periphery. We are of the opinion that the lesion has become active as a result of recent infection, as indicated by the bacterial findings, extensive necrosis, peritonitis, and nephritis. The old adhesive peritonitis probably occurred at the time that the abscess was primarily active. The age of the thrombosis and hepatic infarction can be surmised only.

The infarction appears to be more recent than the extensive thrombosis, and particularly the thrombosis of the vena cava, would indicate. We believe that the older part of the thrombus is in the vena cava, and the hepatic thrombi are more recent, probably dating from the last infection. We admit that the extensive

necrosis, particularly marked in the left lobe, may have resulted from the infection without coincident infarction, but think that the many plugged veins and the perilobular and intralobular extravasations afford the picture of an infarct. *December 12, 1901.*

CANCER THROMBUS IN BRANCH OF HEPATIC VEIN, WITH INFILTRATION OF WALL.

BY W. M. L. COPLIN, M.D.,

AND

L. H. PRINCE, M.D.

(From the Laboratory of the Jefferson Medical College Hospital.)

This specimen was observed in a cancer of the liver secondary to cancer of the pylorus. There is nothing unusual in the secondary nodules in the liver, but on incising the organ there was found a large hepatic vein, nearly 0.5 cm. in diameter, upon one wall of which there was noted an elongation nearly 2 cm. in length, thinning off at either end, and possibly 5 mm. in thickness near its center. It extended around the lumen of the vein to a distance of approximately 0.5 cm.

We were curious to know whether it was an involvement of the vein that had extended into the surrounding tissue, or involvement of the vein from the surrounding tissue. The indications all pointed to the latter view.

A small portion of the wall of the vein containing the thrombus was removed, and serial sections were made.

These show that the intima of the vein is no longer recognizable under the thrombus; that the fibrous and elastic layers are involved by the new growth, which rests directly upon the subendothelial tissue. Stains for elastic tissue yielded only negative results.

The thrombus is made up of typical cancer, with an abundant collagenous stroma and small alveoli packed with epithelial cells.

Smaller alveoli are to be recognized in the vein wall, although they are not abundant, and around the vein the cancer presents no unusual feature. It is clearly an instance of cancerous involvement of the vein from the adjacent cancer nodule. Serial sections show that the point of nodular invasion of the venous wall is truly small, and that the cancerous thrombus extends as a plate along the axis of the vein almost as far against the blood stream as with it. Where the thrombus spreads out over the vein the endothelium of the intima is absent; the surface of the cancer thrombus bears neither clot nor endothelial covering.

December 12, 1901.

FATTY CIRRHOSIS IN THE LIVER OF A DOG.

BY W. M. L. COPLIN, M.D.,

AND

L. H. PRINCE, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

The specimen is that of a dog's liver, removed from the animal in the anatomical laboratories of the Jefferson Medical College during the special course given in comparative anatomy.

The dog was a mongrel, male cur, brownish in color, well nourished, the muscles normally colored and possessing an abundance of adipose tissue. Death had been brought about by asphyxiation with illuminating gas.

An ascites estimated at between one and two liters was present. Careful examination disclosed no gallstones nor evidence of any other obstructive lesion, past or present. The liver was not adherent to the diaphragm or to any of the surrounding viscera. The organ was firm and resistant upon palpation, and weighed 195 grams.

The liver consists of six lobes (one was removed for histologic study). It possesses a markedly granular, or, possibly better, a "hobnail" surface. The smaller lobes, and particularly the under surfaces of both large and small lobes, present this appearance more conspicuously than the diaphragmatic surfaces. These tuberculous projections are on the average of about 3 mm. in diameter and possibly 1 mm. high.

Here and there on the diaphragmatic surface of the superior and larger lobe one observes the presence of nipple-like elevations, each surrounded by a very narrow depression about 1 mm. in depth. The surfaces of these elevations are minutely granular. A few decidedly puckered scar-like depressions are also noted.

The edges of the lobes are sharp, with occasional indentations, varying from 0.5 mm. to 2 mm. in depth.

The ground color originally was a light reddish-brown, with a mottling of yellow and dark-red irregular spots from 1 mm. to 5 mm. in diameter. The yellow spots predominate, and fade almost imperceptibly into the ground color. The red spots were more sharply outlined, and occasionally could be seen merging into the yellow areas. This color picture could be most clearly seen on the freshly cut surface. One could not determine with certainty, macroscopically, the presence of fibrous tissue, although the presence of a number of pale, rather hyaline linear markings seemed to suggest it.

The gall-bladder is observed to be distended and to extend 2 cm. beyond the border of the lobe. The bile is a somewhat copper-colored, slightly viscid fluid. Quantity, 10 c.c.

Specimens were fixed in picrosublimate solution and infiltrated with paraffin. A further number of specimens were treated with Flemming's solution and infiltrated with paraffin and celloidin. Sections were stained with hematoxylin and Van Gieson's mixture, toluidin blue, etc.

Histology. For some reasons not determined by the writers—although the same condition has been observed in other organs from man, and animals killed with coal gas—fixation is imperfect, infiltration difficult, and sections extremely fragile. The organ contains a notable increase of connective tissue distributed in a most irregular manner; in some areas the connective tissue is old; these areas are small and infrequent, but little of the connective tissue having reached that age which fully formed fibrils elect Van Gieson's stain.

The older masses of fibrous tissue are near the portal canals and surround the larger branches of the portal vein and some of the larger bile ducts. Occasionally strands of wavy fibrillated tissue, electing Van Gieson's stain, can be seen traversing the intralobular areas as finer bands. Such masses, however, are scarce. The fibrous tissue between the lobules is clearly of recent formation. In many areas the cells are still lymphoidal, but for the most part the young connective tissue takes the form of spindle elements, long and short, possessing ovoidal nuclei.

The distribution of the fibrous tissue is also unusual. In some areas groups of lobules are surrounded by bands of fibrous tissue, 1 mm. or 2 mm. in diameter, and occasionally such masses will be quite free from fibrous tissue between the lobules. The condition in such areas is practically that commonly called polylobular cirrhosis. In other areas individual lobules are surrounded (monolobular cirrhosis), and in still other areas the connective tissue can be seen entering the lobules, and sometimes approaching almost to the central vein (intralobular cirrhosis).

The amount of fat in the liver cells is most conspicuous. For the most part the fat is at the periphery of the lobule, although this is by no means a constant phenomenon, as some of the lobules contain centrally placed areas of fat. The fat is best seen in the osmicated preparations, although, unfortunately, Flemming's solution has penetrated but little. The irregularity in location is here admirably shown. The intracellular location of the fat shows nothing unusual. Many of the liver cells not containing fat appear small and shrunken. Around some of the bile ducts there is an increase in the connective tissue, and occasionally this tissue is old, but for the most part comparatively recent. The biliary epithelium shows in many areas desquamative changes. Occasionally it is necrotic and lying free in the bile vessels. In still other biliary ducts granular acidophilic material can be found in their interior. Quite a number show no abnormality.

Diagnosis and Remarks. The condition is clearly one of fatty

cirrhosis, with an unusual distribution of the newly-formed connective tissue. The cirrhosis may be said to be in some areas polylobular, in other areas monolobular; and while, for the most part, it is perilobular, it is occasionally intralobular. Evidences of proliferation of the biliary ducts is wanting. Fatty infiltration is conspicuous. It is not possible to give the cause, but the findings indicate that the lesion must be regarded as consecutive to a cholangitis non-suppurative in character.

December 12, 1901.

HEART SHOWING CHRONIC TUBERCULOSIS OF THE PERICARDIUM, WITH INVOLVEMENT OF THE MYOCARDIUM.¹

BY

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(From the Laboratories of the Jefferson Medical College Hospital.)

The specimen was obtained at autopsy from the body of a male negro, aged 24, who died in October, 1902. In March of that year he had an attack of pneumonia, from which he never fully recovered, the succeeding symptoms being pain in the chest, cough, copious expectoration, night sweats, and progressive weakness. He was admitted to the hospital August 15, 1902. The notes state that the action of the heart was then rapid, but there was no murmur. The pulse was weak. The upper portion of the left lung was flat on percussion, this flatness changing on August 25 to high-pitched tympanitic resonance. Repeated examinations of the sputum for tubercle bacilli were negative until August 27, when they were demonstrated to be present. A note on October 6 states that the heart was not displaced and that the sounds were normal. On October 14 the patient died suddenly while in the dining-room.

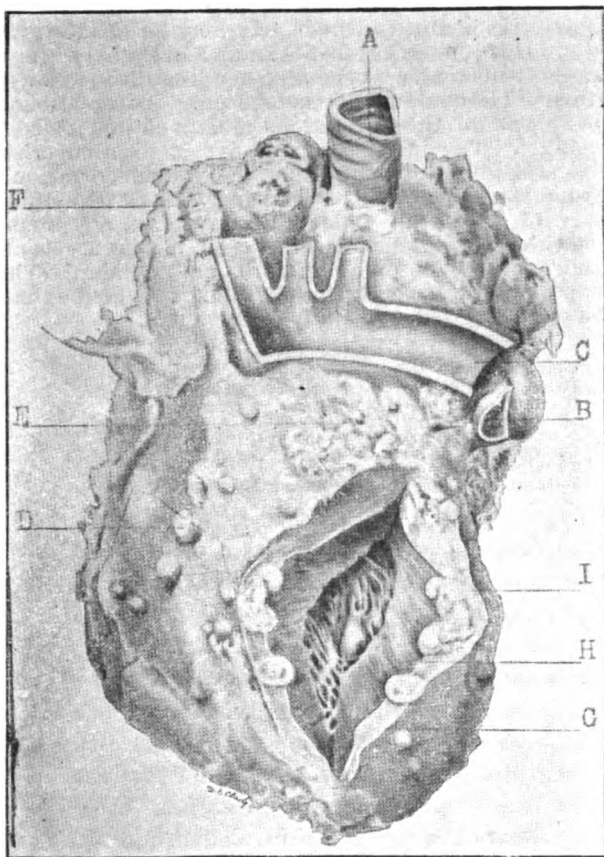
Autopsy showed the mediastinal tissues to be studded with variously-sized grayish or yellowish nodules, some of which had caseous centers. The heart and the mediastinal tissues formed practically one large adherent nodular mass. Both pleuras were universally adherent. In freeing adhesions upon the left side, the lung, which was markedly caseous and contained many cavities, was extensively torn. The pericardium is universally adherent, the external surface being studded with yellowish nodules, varying from 0.2 to 2 cm. in diameter. In a number of places these nodules extend into the heart muscle, in some instances to a depth of

¹ Read at the Philadelphia Pathological Society, March 12, 1903.

more than a centimeter. The involvement of the heart is greatest in the left ventricle, but is quite extensive in the right. The liver, spleen, pancreas and kidneys contain miliary tubercles.

Microscopic examination shows the adhesions uniting the two layers of the pericardium to be formed of granulation and fibrous tissues in which are disseminated areas of caseation. At many points the visceral pericardium has disappeared, and the heart muscle shows invasion by lymphoid cells or even granulation and fibrous tissues. Sections from a dozen blocks have been examined, but in none of them have structures bearing any resemblance to an anatomic tubercle or a giant cell been found. A very few tubercle bacilli were found in one section.

Tuberculous pericarditis is not a notably infrequent condition, this specimen being presented because of the extent rather than the nature of the lesion. In 1,048 autopsies Wells¹ found tuberculous pericarditis ten times and Baginsky reports fifteen cases in 4,500 autopsies. Robinson² reports two cases, and fully discusses diagnosis and treatment. Riesman³ reports a case of primary tuberculosis of the pericardium, and states that the primary form is rare, the most frequent source of infection being a tuberculous mediastinal or bronchial lymph gland, which was in all probability the source in this instance. To Riesman's article is appended a full bibliography. Sabin⁴ reports a case in which recovery followed repeatedappings of the pericardium and the right pleura. Tubercle bacilli were found in the pericardial, but not in the pleural, effusion. Robinson states that tuberculosis as found in the pericardium is generally either of the miliary form or cheesy masses, though in certain instances there is no evidence of tuberculous deposit in the adhesions present. The myocardium may be affected at the same time as the pericardium, the former coming primarily, as a rule, from the latter. The caseous form penetrates deeper and may perforate the cardiac wall. Myocardial tuberculosis, however, is rare, Anders⁵ collecting from literature but 71 cases, to which he adds one of his own. He states that Valentin found 7 cases of myocardial tuberculosis in 3,203 autopsies, and Sangalli 2 cases in autopsies upon 796 tuberculous patients. With the statement of Wells, corroborated by Osler, that "tubercular pericarditis is generally unaccompanied by any symptoms referable to the heart, and is almost always an autopsy finding,"



Chronic, adhesive, indurative and caseous tuberculous mediastino-pericarditis. Heart and adjacent mediastinal structures. (Four-ninths natural size.) A, trachea slightly distorted by pressure. B, left bronchus, compressed by enlarged peribronchial lymph-nodes. C, aorta; the arch is displaced to the right; the middle of the arch is elongated largely at the expense of the descending portion; it is probable that a large part, but certainly not all, of this distortion is postmortem. D, one of several caseous lymph-nodes on the mediastinal aspect of the pericardium; some of these nodules are indistinguishable from caseous masses that have arisen in the pericardial synchia. E, area of caseous tuberculosis occupying fissure between the left auricle and corresponding ventricle. F, caseous mediastinal (peritracheal) lymph-nodes. G, thickened and adherent parietal layer of the pericardium. H, thickened visceral layer of the pericardium (epicardium); the space between F and G is occupied by firm, greyish, slightly hyaline fibrous tissue in which are embedded many caseous areas. I, caseous mass extending into the myocardium; even in this short incision, through the lateral wall of the left ventricle, several points of myocardial invasion can be seen.

Robinson is inclined to differ. It may be of interest to note in this connection that Ferrand and Rathery⁶ report a case of tuberculous vegetative endocarditis following primary tuberculosis of the spleen. Tubercle bacilli were found in the vegetations and in clotted blood in the heart. The question of adhesive mediastinopericarditis arises in this connection, but its consideration is beyond the scope of this brief paper. A careful clinical study of a case in which this condition, presumably tuberculous in origin, was diagnosed, has been recently published by Gibson, Bullmore, and Conder.⁷ They compare their case with those of Harris,⁸ whose exhaustive work is based on a study of 25 cases.

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- ⁵ Jour. Am. Med. Assoc., November 1, 1902.
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- ⁷ *The Practitioner*, February, 1908.
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A CASE OF ENDOTHELIOMA OF THE ORBIT.¹

BY C. A. VEASEY, A.M., M.D., PHILADELPHIA,

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The following case of orbital growth presented himself at the Jefferson Medical College Hospital on July 8, 1901, for examination and treatment:

History.—H. R. P——, married, a male, aged 35 years, is a chemist by occupation. According to the patient's statement his mother died from "cancer of the tongue." His father had an enlargement on the cheek bone, but as it caused him no annoyance nothing was ever done for it. One brother died of pulmonary tuberculosis. The patient himself is tall and slender, his general health being good. Twelve years before the examination a small growth about the size of a green pea was observed beneath the left upper eyelid at the external portion of the orbit, and in front of the location of the lacrimal gland. The size of this growth slowly increased until it became as large as a walnut. At this time he consulted some oculist at a hospital dispensary, where the condition was diagnosed as a prolapsed lacrimal gland.

Examination showed a kidney-shaped growth, situated beneath the outer third of the left orbital ridge, which was mobile from side to side, but apparently having deep attachments in the orbital cavity. The eyeball was pushed slightly toward the nose and downward, and there was some impairment of the upward movement. No ophthalmoscopic change was found, and the vision of each eye was normal. During the year preceding this examination the growth of the tumor had been much more rapid than before.

Operation.—Extirpation was advised, and as the patient refused to have employed any general or local anesthetic, the tumor was dissected out without their use through an incision along the orbital ridge in the outer third of the lid. Very little difficulty was experienced in its removal except that the point of attachment was deep in the orbital cavity, from which it had to be divided with scissors. There has been no recurrence of the growth.

The specimen was sent to the pathological laboratory of the

¹ Read at the thirty-eighth annual meeting of the American Ophthalmological Society at New London, Conn., July 16, 1902.

Jefferson Medical College, and under the direction of Prof. W. M. L. Coplin sections were made and a report submitted.

Macroscopical examination showed the growth to be kidney-shaped, measuring $2\frac{1}{2}$ centimeters in length, and from 1 to $1\frac{1}{2}$ centimeters in width. It was hardened in a three-per-cent solution of formalin, and was firm in consistency, cutting with little resistance. The outer surface is smooth and of a slate color, with grayish mottling. The inside surfaces present a granular appearance, one-half of these surfaces being dark-gray with blackish, yellowish, and brownish mottling, while the remainder is light-gray in color. If pressure is brought to bear upon the latter half a grayish gelatinous material exudes, giving to the surface a honey-comb appearance. In the dark-gray half of the inside surfaces are three black areas containing gelatinous material, each measuring approximately two millimeters in diameter, two of these areas being

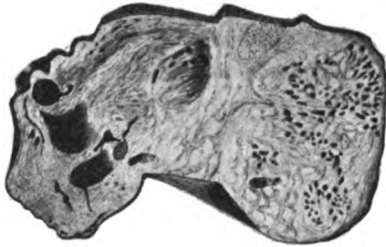


PLATE I.—Endothelioma of the orbit. Macroscopical appearance of incised surface. The growth was half the size of the reproduction.

partially surrounded with a narrow rim of grayish, translucent, jelly-like substance. The mass is completely encapsulated. After dehydrating in alcohol and embedding in paraffin the sections were stained with hematoxylin and eosin, picric acid, toluidin blue, by Van Giesen's method and for hyalin material.

Microscopical Examination.—Sections made from the light-gray half of the mass are covered on three sides by a layer of fibrous and muscle tissue, the width of the layer varying from one to two millimeters in thickness. It contains areas of rhexis, and scattered through it is a small amount of blood pigment. It also contains a few small round connective tissue cells and a number of large cells that take eosin intensely, but do not take any basic stain. At one end of the growth there is an area of gland structure in the fibrous layer, but between this and the tumor proper the capsule is found unbroken. The gland structure presents the ordinary appearance of normal lacrimal gland.

Within the capsule the structure is composed of fibrous and muscle tissue and finely reticulated network that stains faintly with the basic dyes. In this structure are what appear to be giant cells, with a low magnification, but with a high magnification it is found that they consist of a number of cells lying very close together. Their nuclei stain intensely with the basic dyes, while the protoplasm stains with the acid dyes. In a number of the cell clusters there is a faintly basophilic intercellular substance; here the nuclei

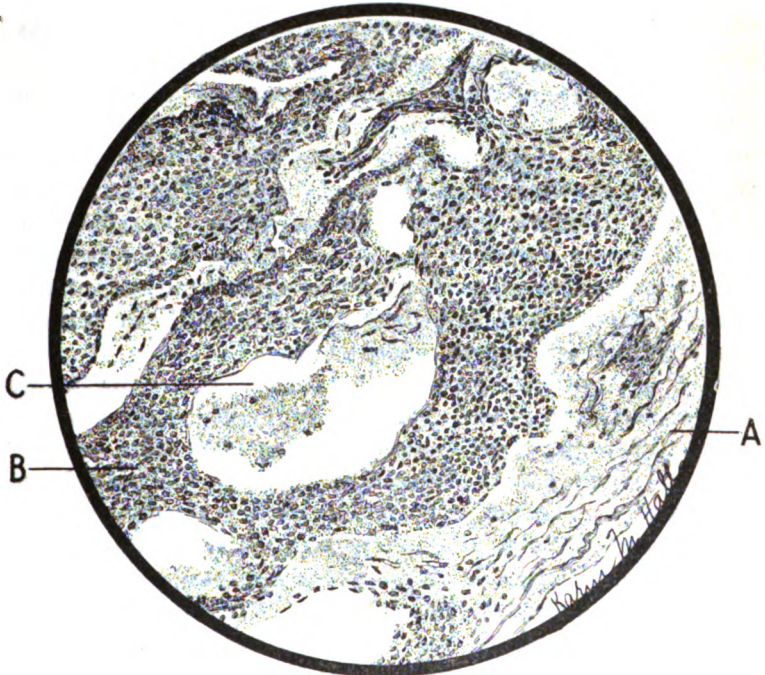


PLATE 2.—Endothelioma of the orbit. Microscopical appearance showing at A, extreme margin of capsule; B, columns of endothelial cells; C, distended lymph spaces containing more or less granular acidophilic material. (Technique: Fixed in formalin, paraffin, hematoxylin and Van Gieson. Obj., B. and L., $\frac{1}{4}$ in., oc. 1 in.)

do not stain so intensely, and the protoplasm is granular and basophilic in character. Throughout the reticulated structure there is also found another type of cell, varying in size from 7 to 20 micromillimeters in diameter, some being oval and others polyhedral in shape. Some of these cells do not take any basic stain, while others take it only faintly. Many anastomosing spindle and stellate cells are also found.

In the dark-gray portions of the growth the cellular elements are more conspicuous. In many of the cells the nuclei are oblong,

resembling the nuclei of muscle fibers, and varying from 8 to 15 micromillimeters in size, and staining intensely with the basic dyes. Some of them are surrounded by a rim of protoplasm, but the greater number appear to lie free in a basophilic granular material. In other situations the nuclei are either oval or spindle-shaped, but are all surrounded by a rim of protoplasm. Many of these nuclei contain vacuoles. Beside these, or near-by, are many spaces that are found to be occupied by a finely granular basophilic material, and are surrounded by a rim of basophilic material somewhat denser than that just referred to. There are also a few scattered areas of hyaline cartilage undergoing myxomatous degeneration.

Throughout the entire sections, but more marked in the periphery, are large areas that are composed of homogeneous acidophilic substance, and within these areas are grouped the cellular masses and mantle-like accumulations of endothelial cells. The microscopical examination, therefore, shows the growth to be a mixed tumor of endothelial origin similar to the mixed tumors of the parotid, to which the term endothelioma has been given; and the general grouping and arrangement of the cells is such as to justify the term used by Borrmann of lymphangio-endothelioma.

Warthin¹ has reported a somewhat similar case having its origin in the lacrimal gland. The patient was a farmer, aged 45 years, whose family and personal history were negative. Five years before the growth was removed by Dr. Fleming Carrow there had been observed a bulging of the right eye, which increased gradually until there was marked exophthalmus. For two years preceding the removal of the growth the increase in size had been very slow. Vision in the right eye was 14-120; in the left 14-20. The eye of the affected side showed neuroretinitis and interstitial choroiditis. The tumor was about the size of a walnut, and was found well back in the orbit in the lacrimal gland region, but its exact relations to the gland could not be definitely determined. The tumor was shelled out of its bed, having no attachments, after which the exophthalmus disappeared, and the vision improved.

The growth was found to possess a thick capsule of dense hyaline connective tissue, from which trabeculæ of a similar tissue passed into the growth, giving it somewhat of a lobulated appearance. Between these trabeculæ the appearance of the cut surface varied greatly, in areas being firm and quite like cartilage, in other portions

¹ Aldred Scott Warthin: "A Case of Endothelioma of the Lachrymal Gland (Myxochondro-Endothelioma Cyindromatodes), with an Analysis of Previously Reported Cases of Lachrymal Gland Tumors." *Archives of Ophthalmology*, vol. xxx, 1901, p. 601.

translucent and jelly-like; other areas were yellowish, granular, and of a crumbling consistency. There were a few small reddish spots scattered over the surface. Immediately beneath the capsule the peripheral portion was pinkish, more homogeneous, and of softer consistency.

The microscopical examination showed the growth to be a mixed tumor, containing myxomatous tissue, cartilage, cylindromatous and sarcomatous areas, similar to the mixed tumors of the parotid. Just beneath the peripheral cellular zone there were scattered gland spaces lined with short columnar or cubical epithelium similar to that of the lacrimal gland. Many of these glands were very irregularly branched, some were cystic, and nearly all contained a colloid substance. A few of these glands were found also in the peripheral zone, but they were most numerous toward the center, where some areas presented the appearance of normal lacrimal gland structure. It is believed, therefore, that this growth had its origin from the lacrimal gland.

The author in his most excellent monograph reviews the literature of lacrimal gland tumors, and states his belief that the great majority of lacrimal neoplasms are mixed growths of endothelial origin similar to his own case, and should therefore be classed as endotheliomata, to accord with the similar tumors of the parotid. It is also stated there can be but little doubt that in all of those reported cases of lacrimal gland tumors in which cartilage, hyaline and myxomatous tissue were present in the growth, the neoplasm was similar or identical with the mixed tumors of the parotid.

In my own case the connection with the lacrimal gland is not so apparent, for while the growth seemed to be so adherent to the gland that a small portion of the latter was excised in its removal, serial sections show that the capsule between the gland and the growth was unbroken. In addition, no gland spaces with epithelial lining are present.

As pointed out by Warthin, the serous gland endotheliomata occur most frequently in early adult life, giving rise to slow-growing painless tumors, which are usually found encapsulated. There seems to be very little tendency to become malignant, and when they have been entirely removed their recurrence is seldom observed.

THE IDENTIFICATION OF THE COLON BACILLUS BY REACTIONS PRODUCED IN CULTURE MEDIA CONTAINING NEUTRAL RED.—OBSERVATIONS ON REACTIONS OF OTHER BACTERIA ON THE SAME MEDIA.*

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It has been stated by several authorities that neutral red agar is a good medium for differentiating the bacillus coli communis from the bacillus typhosus. Furthermore, it has been claimed by Rothberger and Hunter, that the bacillus coli communis upon this medium produces a fluorescence and that the medium is turned to a yellowish color—nearly a canary yellow.

Neutral red (neutral roth) according to Lee¹ is a basic color. The term "neutral" refers to the hue of its solution and not to its chemical composition. Its neutral red tint is turned bright red by acids, and yellow by alkalies.

From the above apparently specific reaction Hunter² claims that he has been able to detect the presence of the colon bacillus in water supplies, by simply inoculating the water upon this medium and obtaining the above reaction. If the test can be relied upon, one can readily see the importance of such a medium for the detection and identification of an organism so closely resembling the bacillus typhosus. As the reaction of the colon bacillus

*Read before the Philadelphia Pathological Society, October 25th, 1901.

**From the Laboratories of the Jefferson Medical College Hospital.

(1) Microtometist's Vade Mecum, 5th ed., 1900, pp. 220 and 221.

(2) London Lancet, March 2, 1901.

was alleged to be characteristic, the writer undertook experiments with other organisms with the object of determining if the colored media yielded any other important differentiating test.

Savage³ uses a 0.5 per cent. glucose neutral red bouillon for the routine examination of water where the bacillus coli is suspected. His method is to add 10 cc. of water to a tube of $\frac{1}{2}$ per cent. glucose neutral red bouillon, then to 40 cc. of water add the contents of a second tube of neutral red bouillon. Incubate at 37° C. and examine daily up to 72 hours. Of 50 waters examined, he is said to have obtained 39 positive results that is, fluorescence and the red color reduced to yellow or orange.

Of 34 waters especially examined for the bacillus coli communis, a positive result occurred in 31 and the organism was isolated ~~therefrom~~ in 31 samples.

Pakes⁴ claims that the same reaction takes place with the *proteus vulgaris*, bacillus prodigiosus, bacillus kiliense, lactis aërogenes, and all the members of the enteritidis of Gärtner and Friedländer groups.

Hunter claims that the bacillus edematis maligni, bacillus proteus vulgaris, bacillus prodigiosus, bacillus tetani, also give the same reaction. He draws the following conclusions:

1. That the bacillus coli communis and a few other micro-organisms possess the power of reducing neutral red to a canary yellow fluorescent color.
2. That the bacillus typhosus never possesses this power of reduction.
3. That it is possible within twelve to twenty-four hours to diagnose with accuracy, by means of neutral red, the typhoid group of micro-organisms from the true colon group.

In the experiments detailed below, the medium was made by using ordinary peptone agar and adding 5 drops of a saturated watery solution of the dye to each tube containing 15 cc. of neutral agar. No definite formula for preparing the medium has

(3) British Medical Journal, Aug. 17, 1901.

(4) British Medical Journal, Aug. 17, 1901.

been published. The medium was then sterilized and allowed to "set" as ordinary slant agar. Inoculations were made upon the medium and the reaction was noticed in the tubes from 24 hours to 5 days. The cultures and controls, with the exception of the bacillus of tetanus, were incubated at 37° C.

The cultures of the bacillus coli communis were as nearly typical as could be desired, and as every one knows that all reactions or characters of a certain bacterium are not constantly obtainable, so one or two characters of this bacterium failed to develop.

In the cultures *a* to *g* the bacilli were all motile; their growth on agar was of a grayish-white color, they all possessed an acid reaction, turning blue litmus milk red, and in cultures *a*, *b*, *c*, *d*, *e* and *f* producing firm coagula, while in culture *g* no coagula were observed.

In bouillon they all clouded the medium and in cultures *a*, *c*, *e* and *f* a delicate pellicle was observed.

Upon potato the growth of all the cultures was of a yellowish-brown color. Gas developed in cultures *c*, *d* and *e*; no gas was demonstrable in the other cultures. Indol was produced in cultures *b*, *c*, *d*, *e* and *f*, but was absent in cultures *a* and *g*.

In series 1, 2 and 3 the bacilli were motile; the growth upon agar was of a grayish-white color, and all possessed iridescence. They all possessed slight acid properties, evidenced by rendering blue litmus milk, pink; coagulation was observed only in tube 1. In bouillon they all clouded the medium and formed a delicate pellicle upon the surface of the medium. Upon potato the growth was of a brownish color. Abundant gas production was present in culture 1, none was present in the other two tubes. Indol was produced in all three cultures.

The bacillus obtained from Dr. Wayne Babcock was motile; the growth upon agar was at first grayish-white in color, and later, light brown. It coagulated milk; in bouillon it clouded the medium, without formation of a pellicle. Upon potato the

growth was of a brownish color. Gas formation and indol production were present.

In two cultures of the writer's the growth upon agar was of a grayish-white color; milk was coagulated, bouillon was clouded, and a pellicle formed on the surface of the medium. Upon potato the growth was brownish in color. Gas formation was present in both cultures. Indol production was present in one and absent in the other. All the bacilli used were negative to Widal's reaction.

Seven cultures of the *Bacillus coli communis* were obtained from Dr. N. Gildersleeve, and lettered from *a* to *g*. These were inoculated upon the neutral red medium and gave the following results:

Bacillus coli communis a: The growth is of a pinkish color, with fading of the color, and a deposit of small red crystals throughout the medium.

Bacillus coli communis b: The growth is of a dark red color, with fading of the color, and the deposit of small red crystals throughout the medium.

Bacillus coli communis c: The growth is of a dark yellowish brown color, with slight fading of the color of the medium and the deposit of small red crystals throughout.

Bacillus coli communis d: The growth is of a light pinkish color, with slight fading of the color of, and the deposit of small red crystals throughout, the medium.

Bacillus coli communis e: The growth is of a very light pinkish red color, with fading of the color of the medium and the deposit of small red crystals throughout.

Bacillus coli communis f: The growth is of a pinkish color, with fading of the color of, and the deposit of small red crystals throughout, the medium.

Bacillus coli communis g: The growth is of a light gray color, with no appreciable fading of the color of the medium.

Another culture obtained from Dr. Wayne Babcock was tried upon the medium. The growth was

of a reddish color and a slight fluorescence developed; there was no fading of the color of the medium. Iridescence was noticed upon ordinary agar.

Three cultures, 1, 2 and 3, of the colon bacillus obtained from Dr. Gilliland (Laboratory of Veterinary Medicine, University of Pennsylvania) were also inoculated into neutral red agar.

Bacillus 1: The growth is of a dark red color, with fading of the color of the medium, and the deposit of small red crystals throughout.

Bacillus 2: The growth is pinkish in color, with slight fading of the color of the medium, and the deposit of small red crystals throughout; later the medium turned to a brownish color, but no fluorescence was observed.

Bacillus 3: The growth is reddish in color, with marked fading of the color of the medium, and the deposit of small reddish crystals throughout.

Iridescence was observed in all three cultures upon glycerin agar. In the series of cultures obtained from Dr. Gildersleeve, *b* and *c*, after 14 days' growth, turned to a yellowish brown color, but no fluorescence was demonstrable.

A second series of experiments was carried out, with the bacillus coli communis and the other organisms named, by melting agar and adding five drops of a saturated watery solution of neutral red, re-sterilizing, and when sufficiently cool, inoculating and incubating at 37° C.

These tubes were not slanted. Plates were also made of the bacillus coli communis and bacillus typhosus with neutral red agar, but there was no essential difference in the behavior of the growths. Each was attended by complete decolorization of the medium, as Hunter has observed, hence there is no differentiating point in plate cultures between the two organisms in question.

In the one series of cultures, lettered *a* to *g* inclusive, the following reactions were noticed after 24 hours:

Culture *c* presented a more or less brownish color,

with slight fluorescence. It resembles the reaction observed when powdered eosin is dropped in water.

Culture *d* presented a dark brown color of the medium, especially at the bottom of the tube; no fluorescence was demonstrable.

In the other cultures, *a*, *b*, *e*, *f* and *g*, no reaction was demonstrable, neither changing of the color of the medium nor fluorescence was seen.

In the series numbered 1 to 3 inclusive the color of the medium 2 had faded; no further reaction was observed.

In 3 a brownish color took the place of the dark red and there was a slight fluorescence observed.

In 1 no reaction was demonstrable.

In still another culture no reaction was observed.

In a culture that was obtained from the feces, a greenish yellow color of the medium was observed at the bottom of the tube, which also possessed the fluorescence mentioned above, but more marked.

In 72 hours the following observations were made:

Culture *c*, mentioned above, presents quite a marked fluorescence, while the color of the medium was more or less reddish yellow.

Culture *f*, while not showing any change in the color of the medium, shows fluorescence upon the surface.

Culture *d* shows very slight fluorescence together with the dark brown color of the medium above mentioned.

In the other cultures, *a*, *b*, *e* and *g*, no reaction was demonstrable.

In 72 hours, in the series 1, 2 and 3, 2 shows a slight fluorescence upon the surface of the medium, 3 shows a marked fluorescence upon the surface and slight fluorescence throughout the medium.

There is no reaction seen in 1.

In Dr. Babcock's specimen no reaction was demonstrable; in the culture obtained from the feces no reaction was obtained; neither fluorescence nor turning of the color of the medium from a red to a yellow color after 72 hours' observation.

It will be seen from the latter experiments that 13 different cultures of the bacillus coli communis were used.

The reactions were noticed after 24 hours, and up to 5 days. In but 7 of the cultures was fluorescence demonstrable, while not one of the cultures showed the canary yellow color described by Rothberger and Hunter. In only one case was marked fluorescence seen.

In 4 cultures the fluorescence was demonstrable in 24 hours, while in the other three this reaction was not observed until 72 hours had elapsed. The reaction is said to take place in 24 hours, and while some did react in this time, many of the cultures did not. Even after 5 days' observation no other changes occurred.

Why this reaction (fluorescence) should take place in the latter experiments and not in the experiments undertaken with slant tubes of agar, is hard to explain. It may be accounted for by the partly anaerobic atmosphere in which the organism is compelled to grow. Supposing this to be the case, the writer then placed the cultures in a Novy jar and subjected them to an atmosphere of hydrogen for 48 hours. No further reaction occurred.

In the experiments with the other organisms the reaction was similar to that obtained in ordinary slant tubes. No fluorescence was demonstrable in any of the tubes.

A third series of experiments was conducted with 0.5 per cent. glucose neutral red bouillon, with 13 different cultures of the bacillus coli communis, and the other organisms named below. The inoculated tubes were placed in the incubator at 37° C. and observed daily for 5 days. In only one tube of bacillus coli communis was fluorescence observed. This reaction and the yellow color described were quite marked.

Not one of the other cultures of bacillus coli communis nor the other organisms mentioned gave the

fluorescence or the reduction of the red color to yellow or orange up to 5 days.

Fading of the color of the medium from red to pink was noticed in 4 cultures of *bacillus coli communis* and 2 cultures each of *bacillus typhosus*, *bacillus prodigiosus* and *vibrio Schuylkilliensis*. After 13 days had elapsed slight fluorescence was present in one culture of *bacillus prodigiosus* and *bacillus fluorescens*.

The following are experiments made upon the same media with other bacteria.

The growth of the *bacillus typhosus* is of a very delicate pink color, with fading of the color of the medium.

Bacillus dysenteriae (Flexner) grows as light reddish colored colonies attended by a slight fading of the color of the medium.

The growth of the *bacillus megatherium* is of a dark red color and attended by fading of the color of the medium.

The *bacillus putrificus coli* also grows as dark red colonies and the color of the medium fades slightly.

The *bacillus figurans* grows as reddish colonies with no appreciable fading of the color of the medium.

The colonies of the *bacillus capsulatus* (Pfeiffer) are of a reddish color, with marked fading of the color of the medium.

The colonies of the *bacillus subtilis* are reddish in color and there is marked fading of the dye, with a deposit of small red crystals throughout the medium.

The growth of the *bacillus prodigiosus* is of a dull pinkish color, with fading, and the deposit of small red crystals throughout the medium.

Monilla conidia grows as reddish colored colonies, with no perceptible fading of the color of the medium.

The growth of the *bacillus* of swine plague is of a pinkish color, with slight fading of the color of

the medium and the deposit of small red crystals throughout.

The growth of the bacillus of tetanus is of a faint pink color; slight fading of the color of the medium occurs. A sterile tube of neutral red agar was placed in an anaerobic condition; there was no fading of the color demonstrable up to 10 days.

The growth of *sarcina aurantiaca* is of a reddish color with slight fading of the color of the medium.

The growth of *sarcina lutea* is of a dark reddish color, with marked fading of the color of the medium.

Sanarelli's bacillus grows as light reddish colored colonies and shows very slight change in the color of the medium.

The growth of the bacillus *pyocyaneus* is of a grayish white color or slightly yellowish; the red color gradually faded from the medium and there was no appearance of any greenish color.

The growth of the bacillus *anthracis* is pink; the medium fades until it becomes colorless in 72 hours.

The growth of the bacillus *mallei* is also of a pinkish color; the color of the medium fades, especially where the growth is marked and piled up.

The growth of the micrococcus *roseus* is of a deep pink color; the color of the medium fades especially where the growth is most marked.

The growth of the bacillus *janthinus* is entirely colorless with fading of the color of the medium.

The growth of the bacillus *diphtheriæ* is of a reddish tint with fading of the color of the medium.

The growth of the pseudo-diphtheria bacillus presents no essential difference from the true diphtheria bacillus.

The growth of the bacillus *mesentericus vulgatus* is deep pink with fading of the color of the medium.

The growth of the bacillus *fluorescens liquefaciens* (water) is of a deep pink color, the medium does not fade; a slight fluorescence appears.

The growth of the leptothrix *epidermidis* is pinkish and the color of the medium fades.

Table of Reactions of *Bacillus Coli Communis* and Other
Organisms upon Neutral Red Agar and One-Half
Per Cent. Glucose Neutral Red Bouillon.

Organisms.	Neutral red agar.	One-half percent. glucose neutral red bouillon.
<i>Bacillus coli communis</i> (a)	—	— +
<i>Bacillus coli communis</i> (b)	—	—
<i>Bacillus coli communis</i> (c)	X	— +
<i>Bacillus coli communis</i> (d)	X	— +
<i>Bacillus coli communis</i> (e)	—	—
<i>Bacillus coli communis</i> (f)	X	— +
<i>Bacillus coli communis</i> (g)	—	—
<i>Bacillus coli communis</i> (1)	—	—
<i>Bacillus coli communis</i> (2)	X	—
<i>Bacillus coli communis</i> (3)	X	—
<i>Bacillus coli communis</i> (B)	X	X
<i>Bacillus coli communis</i> X	—	—
<i>Bacillus coli communis</i> Y	X	—
<i>Bacillus anthracis</i>	— +	—
<i>Bacillus Mallei</i>	— +	—
<i>Micrococcus roseus</i>	— +	—
<i>Bacillus janthinus</i>	— +	—
<i>Bacillus diphtheriae</i>	— +	—
<i>Pseudo-diphtheria bacillus</i>	— +	—
<i>Bacillus mesentericus vulgatus</i>	— +	—
<i>Bacillus fluorescens liquefaciens</i>	X +	X +
<i>Leptothrix epidermidis</i>	— +	—
<i>Diplococcus</i> (pink)	— +	—
<i>Bacillus Havaniensis</i> (Sternberg)	— +	—
<i>Bacillus of fowl enteritis</i>	— +	—
<i>Staphylococcus pyogenes aureus</i>	— +	—
<i>Staphylococcus pyogenes albus</i>	— +	—

X Fluorescence. — No fluorescence. + Fading of color of the medium.

Table of Reactions of *Bacillus Coli Communis* and Other
Organisms upon Neutral Red Agar and One-Half
Per Cent. Glucose Neutral Red Bouillon.

Organisms.	Neutral red agar.	One-half percent. glucose neutral red bouillon.
<i>Bacillus hematoïdes</i>	— +	—
<i>Spirillum</i> of Asiatic cholera	— +	—
<i>Vibrio</i> Metchnikovi	— +	—
<i>Spirillum</i> of Finkler and Prior	— +	—
<i>Bacillus typhosus</i>	— +	— +
<i>Bacillus dysenteriae</i> (Flexner)	— +	—
<i>Bacillus tetani</i>	— +	—
<i>Sarcina aurantiaca</i>	— +	—
<i>Sarcina lutea</i>	— +	—
Sanarelli's bacillus	— +	—
<i>Bacillus megatherium</i>	— +	—
<i>Bacillus putrificus coli</i>	— +	—
<i>Bacillus figurans</i>	—	—
<i>Bacillus capsulatus</i> (Pfeiffer)	— +	—
<i>Bacillus subtilis</i>	— +	—
<i>Bacillus prodigiosus</i>	— +	X +
<i>Bacillus</i> of swine plague	— +	—
<i>Bacillus pyocyaneus</i>	— +	—
<i>Proteus vulgaris</i>	— +	—
<i>Vibrio</i> Schuylkilliensis	— +	—
<i>Bacillus alcaligenes</i>	—	X

X Fluorescence. — No fluorescence. + Fading of color of the medium.

The growth of a pink diplococcus (obtained from water) is of a deep red color and the fading of the color of the medium is marked.

The growth of the bacillus *Havaniensis* (Sternberg) is deep red and the color of the medium fades but slightly.

The growth of the bacillus of fowl enteritis is pinkish and the color of the medium fades.

The growths of the staphylococci pyogenes albus and aureus were of pinkish color and the color of the medium faded in each case.

The growth of the bacillus hematoïdes is deep pink or almost reddish while fading of the color of the medium is conspicuous.

The growth of the vibrio Schuylkilliensis is of a light pinkish color, with slight fading of the color of the medium.

The growth of the spirillum of Asiatic cholera is of a light pinkish color, with marked fading of the color of the medium.

The growth of the vibrio Metchnikovi is light yellow and the medium fades slightly.

The writer's conclusions are:

1. That, while not affording a specific reaction in the case of the bacillus coli communis, neutral red agar should be classed as a valuable differentiating medium.

2. The typhoid bacillus, while it does not cause a fading of the color of the medium, never gives rise to the fluorescence noticed in some cultures of the bacillus coli communis.

3. Further, the test medium should not be depended upon as the only differentiating one in the examination of water, as several very common bacteria found in water give the same reaction.

The writer wishes to express his thanks to Drs. N. Gildersleeve, Gilliland and Babcock for cultures of the bacillus coli communis used in the experiments. The writer also wishes to thank Dr. Bergey for several cultures of other bacteria.*

*Note:—Since this paper was read the papers by Makgill and by Savage have appeared in the Journal of Hygiene, Vol. I, No. 4, pp. 430 and 437.

UTERUS, GROSS SPECIMEN AND SECTIONS, ALSO SECTIONS OF THE LIVER, KIDNEY, AND BLADDER, FROM A CASE OF PUERPERAL SEPSIS DUE TO MIXED INFECTION BY THE COCCI OF SUPPURATION AND THE BACILLUS COLI COMMUNIS AND OTHER ORGANISMS—ALSO A PRELIMINARY CONSIDERATION OF A MORBID PROCESS AFFECTING UNSTRIPED MUSCLE (PARTICULARLY THE ELASTICA), NOT HERETOFORE DESCRIBED.

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[From the Laboratories of the Jefferson Medical College Hospital.]

*Abstract of Clinical History.*¹ — Mrs. O——, aged 20 years, American; admitted to Jefferson Maternity third day of labor, after repeated unsuccessful attempts at forceps delivery. Condition on admission: Temperature 97°; pulse 150; respiration 26; shock; slight delirium; uterus in state of tonic contraction; bladder greatly distended. Albuminuria, with finely granular and hyalin casts; urea 1.1 per cent; bacteria numerous. Vertex presenting. Highly contracted justo-minor pelvis. Usual treatment of shock. As thorough asepsis as possible; catheterization; craniotomy; delivery, fetus macerated. Uterine cavity curetted and packed with iodoform gauze. Transfusion; hypodermoclysis (repeated); stimulation; one intra-uterine douche. Exhaustion, death, second day after delivery.

Autopsy held ten hours after death. Anatomic diagnosis: Hemorrhagic and suppurative peritonitis; acute splenitis; diffuse nephritis; renal infarction (anemic); pyelitis; ureteritis; cystitis (partly hemorrhagic); septic metritis (puerperal); acute gastric dilatation; focal necroses in liver. Cause: Infection. Organisms found: staphylococcus pyogenes aureus, bacillus coli communis, diplococcus pneumoniae, bacillus diphtheriae (?).

Body of a well nourished female. Marked rigor mortis. Extensive suggillation over posterior part of trunk. Over the anterior abdominal wall and extending laterally are numerous subcutaneous

¹ For the privilege of using the clinical history in this case I am indebted to Prof. E. P. Davis.

hemorrhages; some are petechial, others more diffuse; none are over 0.5 centimeter, and majority scarcely more than 2 millimeters in diameter. Just below the right iliac crest is an old fibrous cicatrix 6 millimeters in length, 4 millimeters in width, its long axis approximately parallel to iliac crest. Skin of abdomen shows usual signs incident to pregnancy; pigmentation in median line conspicuous.

Subcutaneous fat normal in quantity and texture. The extra-peritoneal fat is edematous.

On opening the peritoneal cavity there is found a small quantity of a brownish-white, flaky fluid (not sufficient to measure). This fluid posterior to the uterus yields an offensive odor; when the organ is raised and the pelvic cavity exposed it is found to contain a fibrinopurulent exudate which surrounds the rectum, occupying Douglas's cul-de-sac and supplying a filmy, grayish-yellow coat over the adjacent structures; the parietal peritoneum is beset with numerous hemorrhages (petechial and diffuse), and is markedly hyperemic; similar areas of rhexis are present over the intestinal coils, but are not abundant.

The spleen is attached by an old capsulitis to the diaphragm; the pulp is rather pale, the Malpighian bodies grayish, and the organ a little softer than normal.

The left adrenal is unusually large and measures 2.5 centimeters in length, 2 centimeters in width, 1 centimeter in thickness, shows areas of hemorrhage, and is somewhat edematous. Weight 10 grammes.

The left kidney is small, resists incision, the cortex is swollen and markedly striated; the capsule strips smoothly, subcapsular vessels are conspicuous, labyrinth and tufts are decidedly hyperemic, the intervening area pale and yellow. The pelvis and ureter are slightly dilated, moderately distended, and on section a mucopurulent fluid escapes.

The right adrenal is a small, club-shaped organ 4 centimeters long, 1.5 centimeters wide, 0.5 centimeter in thickness; it presents nothing noteworthy.

The right kidney cortex shows changes similar to those described as present in the left, the pelvis and ureter are distended, the former but slightly if at all dilated; contents same as on left side. The ureter presents an irregular sausage-like dilatation extending to the bladder; its size when distended is about that of a large thumb. About the middle of the kidney is an irregular, pale-white area involving most of the medullary portion. It is fan-shaped, the apex corresponding to the apex of the pyramid and radiating toward the cortex, which is partly involved; this is evidently an area of coagulation necrosis possessing the gross characters of an irregular anemic infarct. [NOTE.—As it was desired to preserve this organ as a gross specimen the area was not removed for histologic study.]

The bladder is moderately distended, reaching 6 centimeters above pubes; its wall is thick, and the veins over the lower part of the organ distended and thrombosed. The mucosa of the bladder is irregularly mottled with purplish spots, which appear to be diffuse areas of hemorrhage situated in the submucosa. The contained urine is opaque, contains flocculi, and is slightly offensive.

The uterus extends to the umbilicus, is slightly pyriform; weight 700 grammes. Organ is flattened in its anteroposterior diameter. Just within the cervix posteriorly is a slough that marks the site of what appears to have been a laceration 2 centimeters in length and 1 centimeter in depth, its long axis corresponding to the axis of the organ; it does not extend through the uterine wall, but the underlying structures are soft, grayish-black in color—in other words necrotic, the necrosis extending to the peritoneal surface posteriorly. There is no solution in the continuity of the peritoneum. The organ is incised on its anterior aspect; the wall, at its thickest point, just above the middle, measures 3.75 centimeters. Fundus measures 1.75 centimeters in thickness.

The interior of the uterus is lined by a grayish-brown, soft, shreddy, necrotic mass of tissue spread quite uniformly over the entire surface of the organ; at points the grayish necrosis extends into the uterine wall to a depth of 0.5 centimeter; it gives off an

extremely offensive odor. Just external to this layer is a grayish zone varying in width; at the fundus it approaches 1 centimeter in thickness, while toward the cervix it scarcely exceeds 4 or 5 millimeters. It is not uniform in breadth, and its outer margin is limited by an irregular reddish line from 1 to 2 millimeters in breadth. The grayish zone is evidently the area of extending necrosis, and the reddish line the limiting area of leucocytic infiltration and vascular dilatation. External to the reddish line the muscle shows no conspicuous gross change.

The peritoneal coat is roughened, red, and injected; over the posterior and inferior surfaces there is a slight, scarcely perceptible, fibrinous deposit that becomes more evident as the lower margins are approached. The ovaries are hyperemic. The Fallopian tubes seem slightly swollen; on opening them the mucosa is found to be reddened, but free from evidence of necrosis or suppuration.

The vaginal mucosa is turgid, at points purplish. Along the right wall extending from the vault downward is an irregular ragged slit with blackish necrotic sides and floor; it is not possible to determine with certainty that this was a laceration, as it seems probable that a similar condition might have resulted from infection and necrosis; it measures 5 centimeters in length. At a number of points the mucous membrane is eroded and necrotic. With the exception noted above the necroses are superficial.

The vulva: The labia are edematous, although not markedly so. The urethral orifice is red and pouting. There is a slight laceration in the perineum. The external genitals and lower part of vagina are in better condition than internal genitalia.

The surface of the liver is beset with whitish areas, presumably areas of necrosis; on incision similar grayish or yellowish-white areas are disclosed; they are for the most part barely perceptible, rarely attaining a diameter of 2 or 3 millimeters. The remainder of the surface shows the usual cloudy swelling. Gall-bladder moderately distended by dark, viscid bile; ducts patulous.

The stomach is enormously distended, extending down to umbilicus. The duodenum is flaccid. Capacity of stomach estimated at

5000 cubic centimeters. It could not be demonstrated that the gastric dilatation was in any way due to kinking on superior-mesenteric vessels and nerve.

The interior of the intra-abdominal alimentary canal manifests no conspicuous abnormality.

The pancreas shows no gross lesion.

Inoculations were made from renal vein, spleen, ureter, and interior of uterus.

Morbid histology: Specimens from the spleen, kidney, liver, uterus, and bladder were fixed, infiltrated with paraffin, and stained by the usual laboratory methods. The stomach was ordered preserved, but unfortunately the instructions were not followed.

Spleen: While this organ contains areas of focal necrosis, they are on the whole less conspicuous and less advanced than those in the liver. The pulp is everywhere distended by erythrocytes, rich in leucocytes, and unusually abundant are the large endothelial cells commonly present in many infectious diseases. As usual these show phagocytic activity, many containing fragmented erythrocytes and pulp cells. The pulp contains pigment and fragmented red cells; the Malpighian bodies are not unusually conspicuous. The fibrous tissue forming the trabeculae is swollen, and the endothelial cells of the sinuses exfoliating and unusually prominent, although karyokinetic figures or other morphologic evidences of active proliferation have not been recognized. The changes seen, as indicated by the foregoing, are those usually found in the spleen subjected to the noxious action of toxic bodies circulating in the blood, and in particular the result of bacterial toxins.

Liver: This organ contains, throughout all the sections examined, multiple necroses. For the most part the areas of necrosis are small, rarely attaining a diameter of 2 millimeters, and in most instances are purely microscopic, involving but a small part of a single lobule. They are usually quite regular, although not constantly so, and are distributed in various areas of the organ, not always involving any part of the lobule, some being situated at the periphery and others more centrally. The hepatic cells are

no longer to be recognized in the centers of the areas of necrosis. Usually toward the periphery can be seen, however, a hazy outline of cells the protoplasm of which is so far disintegrated that it no longer elects even such strongly acid dyes as eosin. The margin of the necrotic area is usually fairly defined, but often it can be observed that the change merges with the surrounding hepatic structure. A few polymorphonuclear leucocytes can be recognized in the areas of necrosis, and an occasional hyalin cell. There are masses of fragmented chromatin, evidently relics of the nuclear contents of hepatic cells. Evidences of regeneration are entirely wanting, and only a few cellular elements of the kind usually grouped among the scavenger cells that are supposed to be influential in removing this dead material are to be recognized. These cells are large, round or ovoidal—of that type described by Chantemesse and Podwyssotsky. The hepatic cells surrounding the areas of necrosis, and indeed practically all the liver cells, are advancedly granular, the cell outlines poorly defined, the protoplasm but faintly staining, the nuclei often indistinct, and in some instances fragmented. The capillaries are singularly free from blood; no evidence of rhexis in the perivascular tissues. The biliary channels, in most of the sections, are difficult to identify by reason of the granular and necrotic changes that have occurred in the canalicular epithelium. The epithelium when still present is usually granular, with poorly staining nuclei, and the cells not infrequently detached and lying within the lumina of the ducts. The endothelium of the capsule is swollen, at points detached, hyalin or advancedly necrotic, evidently participating in the associated peritonitis.

Kidneys: The blood-vessels of the capsule are intensely engorged, and at a number of areas immediately beneath the capsule accumulations of lymphoid cells are to be observed. Occasionally there is a small subcapsular extravasation; such areas of rhexis are, however, infrequent and minute. The changes observed in the cortex are for the most part restricted to the areas of the labyrinth. The epithelium of the convoluted tubules is often granular, desquamating, the margins of the epithelial cells no longer defined, the nuclei fre-

quently hazy, poorly staining, and in some instances the entire cell detached from the basement membrane. The lumina of these tubules almost constantly contain a finely granular, strongly acidophilic detritus, probably partly exudative in point of origin, but presumably, for the greater part, formed from fragmented protoplasm derived from disintegrated epithelial cells that have fallen into the tube. The intertubular tissue is often swollen, and in some instances occupied by lymphoid and plasma cells, the former predominating. The straight tubules of the cortex have not escaped changes similar to, though less in degree than, those already described as present in the convoluted tubules. The tuft changes are variable; some of the tufts are swollen, quite filling the capsule, others somewhat shrunken. In practically all of them there is a conspicuous excess of nuclei apparently belonging to cells largely, if not wholly, of the lymphoid type. Some of the tufts have retracted, or are compressed by a finely granular, intensely acidophilic material occupying the space between the tuft and external capsule.

The tubules of the medullary pyramids (Malpighian tubes, loops of Henley, etc.) are not profoundly altered, the epithelium does not stain with its wonted intensity, nor is its protoplasmic outline accurately preserved; many of the nuclei are diffusely stained, and but dimly outlined. The intertubular connective tissue is hyperemic, the vascular distention being more marked than in the cortical portion, in which blood-vessels are but moderately filled.

The pelvis of the kidney, the ureter, and the bladder show practically the same alteration; it is most advanced in the last named organ, which alone will be described.

Bladder: At no point in the vesical mucosa is the epithelium normal. For the most part it has exfoliated or is exfoliating, necrotic, staining poorly, its cells granular, often hanging by loosely attached necrotic shreds to the underlying structures. Beneath the epithelial layer the connective tissue matrix is swollen, hyalin, infiltrated by leucocytes, mostly of the polymorphonuclear type, and in a number of areas showing distinct hemorrhages. Sometimes along the entire margin of the submucosa for from 0.1 to 0.5 centimeter a

diffuse erythrocytic massing can be recognized, although it is impossible to detect lesions in the vessel walls from which the erythrocytes have escaped. In some of the smaller blood-vessels adjacent to the mucosa the endothelium is swollen, and occasionally leucocytic margination can be recognized. Swelling is evident between many of the complexes or fasciculi in the muscle layer of the bladder, but such swollen tissue is usually quite free from leucocytes.

One of the most interesting conditions observed in this organ, and so far as the writer is aware not previously described in discussion of changes resulting from infection, is a type of hyalin or necrotic change clearly of the same kind as has been frequently observed and accurately described as occurring in the myocardium. In areas showing this change the following alteration can be found:

As will be evident later the appearances of the morbid process observed in the areas where the change is most evident are greatly influenced by the stain used. When the sections have been treated with the usual nuclear dyes—combinations of hematoxylin or carminic acid, thionin, toluidin blue, safranin, Unna's polychrome blue, or alkaline methylene blue, or similar basic dyes preceded or followed, as may be appropriate, by acid dyes—the results attained may be summarized as follows: The change does not appear to involve all of a muscle bundle (smooth muscle complex). In one instance less than one-half of a large band, itself less than 2 millimeters in diameter on transverse section, is involved. Under very low magnification it is easily seen that the involved portion of the muscle band containing a large number of fasciculi elects acid stains with intensity, while the remaining portion of the band possesses its normal tingibility.

Under a higher magnification (25 mm. obj. No. 1 eye-piece) it is seen that in this particular band the area involved has lost its sharp differentiation from surrounding fasciculi. The usual narrow, rather clear space that surrounds the normal complex is now occupied by a quite hyalin acidophilic substance.

Under still higher magnification it is observed that within the complexes the delicate connective tissue—protoplasmic bridges (?)

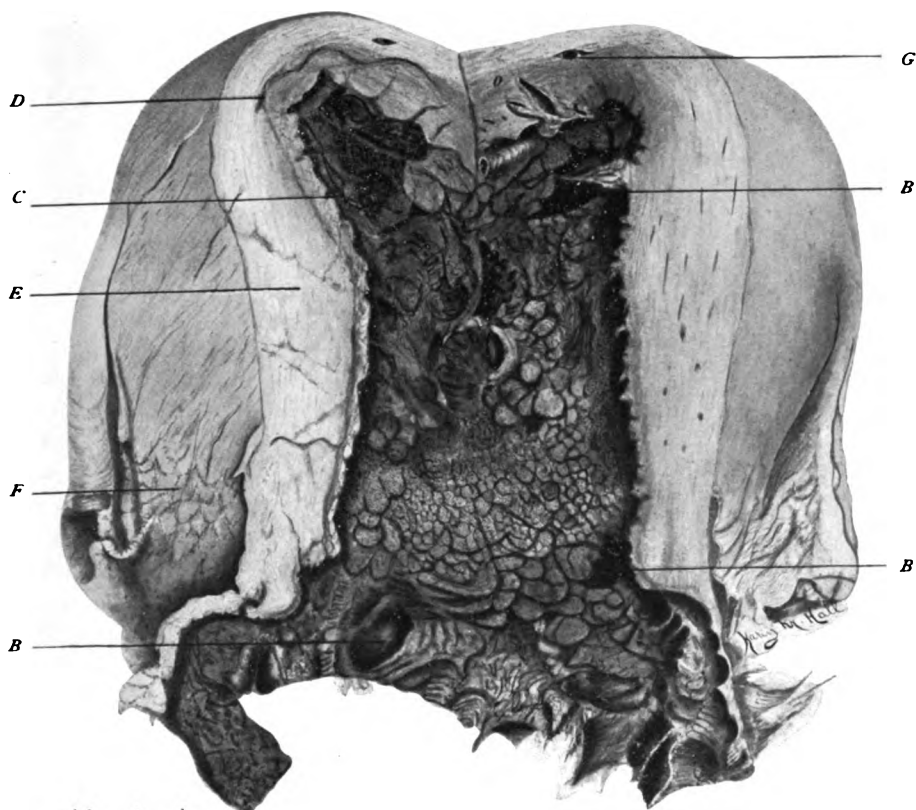


FIG. 1.—Uterus laid open by incision through anterior wall. *A*, Scale, 1 inch. *B B B*, Cavities formed by extensive necrosis. *C*, Necrotic zone that, on its inner surface, projects as a shaggy layer, fragmenting stratum, and externally is bounded by *D*, the line of hyperemia and leucocytic accumulation (see Fig. 2). *E*, Muscle layer not presenting any conspicuous gross lesion. *F*, Peritoneal surface: early stage of serofibrinous inflammation (the block of tissue from which the microscopic drawing was prepared was taken from just above this point). *G*, Thrombosed sinus.

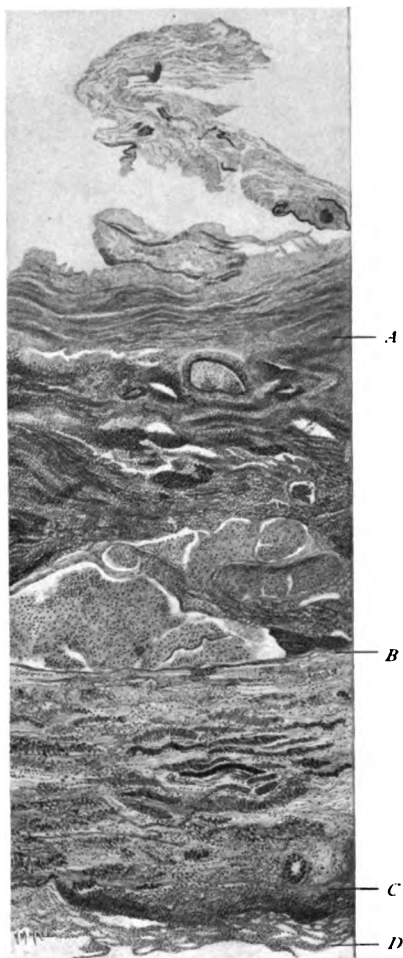


FIG. 2.—Uterus, fixed in Zenker's fluid; paraffin, eosin, and toluidin blue. (Obj., Leitz 16 mm., oc. compensation, and reduced two-thirds.) *A*, Above this point is the necrotic layer consisting of granular detritus containing enormous numbers of bacteria (see text), fragmenting histologic elements, and leucocytes. *B*, From *A* to *B* is the zone of hyperemia, leucocytic invasion, and progressing mycotic infiltration. Numerous uterine sinuses are shown, as well as arteries, all occupied by thrombi. *C*, From *B* to *C* muscle showing hyalin (?) change. This part of the section is only a narrow rim of the actual muscle; nothing would have been gained by showing the entire thickness. Just above and to the left of *C* is an artery the endothelium of which is proliferating. *D*, From *C* to *D* is shown the greatly altered serous covering. The layer represented in the drawing is largely composed of fibrin with entangled leucocytes and endothelial cells.

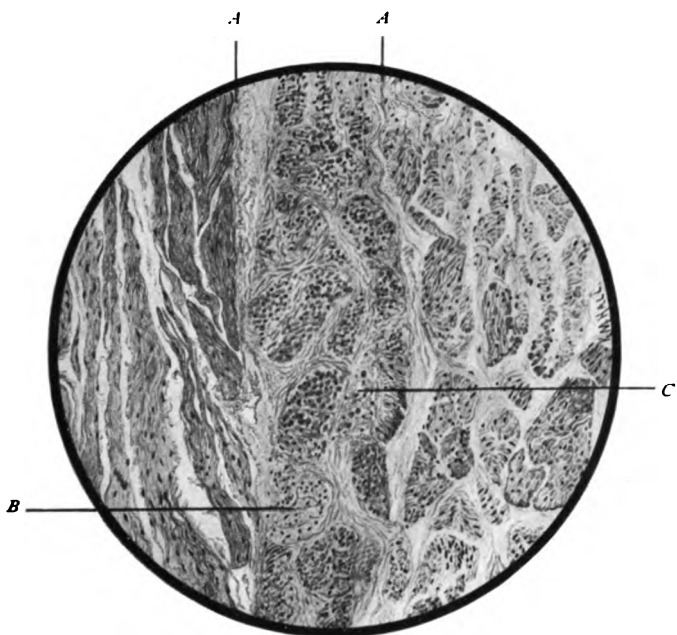


FIG. 3.—Bladder fixed in Bensley's solution, paraffin infiltration, stained with eosin followed by thionin. Composite field built up from different areas in the same section. (Obj., Leitz 16 mm., apochromat. compensating oc., reduced nearly one-half.) *A A*, Between these letters is a band extending vertically through the field and showing the most marked hyalin change. *B*, Area with marked intrafascicular hyalin change. *C*, With eosin and thionin this area appears granular, electing the acid dye. Between *C* and *A* is the larger part of a quadrant in which the nuclear fragmentation swelling and necrosis is marked; there is, however, less hyalin.

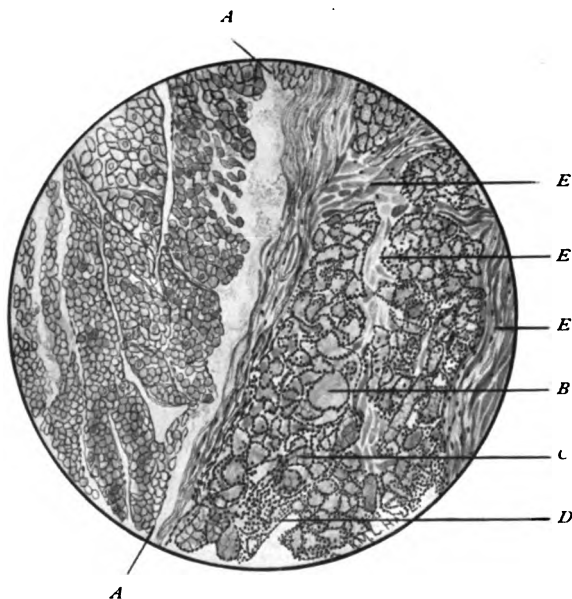


FIG. 4.—Bladder wall fixed in Bensley's solution, paraffin infiltration, stained by Weigert's method for elastica, followed by carmalum and picric acid. (Obj., 2.5 mm., homo. im., compensating oc., and reduced one-fourth.) *A A*, That part of the field lying to the left of leaders from these letters represents the practically unaltered fibers on transverse section. Cells sectioned through the nuclear areas show contained nucleus. The delicate pericellular structure electing the stain for elastica is shown. The area to the right contains a part of the muscle complex manifesting the change described in the text. The beaded elastica is universal; the smooth delicate fibrils shown in the normal field are absent. *B*, Greatly swollen cell. *C*, Fragmenting cell. *D*, Area from which muscle cells have largely disappeared. *E E E*, Swollen connective tissue that at points is granular.

—between the individual muscle cells is now replaced by a hyalin homogeneous acidophilic structure that quite obscures the individual fibers. The condition of the cells in the area involved varies at different points, and even adjacent cells show slightly different changes. The interpretation of the changes within the cells is rendered somewhat difficult by the fact that on transverse section no two cells are divided in exactly the same plane, and hence juxtaposed elements might manifest precisely the same changes, but appear different by reason of the position in the cell through which the section passes. I have not been able to secure a fully longitudinal section of a fasciculus showing the alteration in question, although some longitudinal bundles present evidences of the change. The transversely incised cells, the incision involving what by position and study of serial sections appears to be the nuclear area, usually show no nucleus, or when present the nucleus stains but faintly or not at all; it is sometimes distinctly fragmented and often irregular, and not presenting its normal sharply rounded outline. Occasionally immediately around the nuclear area is a clear space, outside of which may be seen a narrow band or simply the ill defined periphery of the cell. In other instances the protoplasm will be found swollen, finely granular, intensely acidophilic, and without evidence of vacuolization. In some cells the nucleus is eccentrically placed; there is a distinct vacuole occupying the major portion of the transversely incised cell. The sharp outlines of the normal muscle cell are frequently lost in the hazy periphery that merges into the hyalin substance to which reference has already been made. Under magnification of 1000 diameters this hyalin substance presents at points granules, and occasionally a resemblance to fibrils. It is usually free from nuclei and cells. It is perfectly clear in some areas that it has resulted in part at least from disintegration of the protoplasmic tips and bridges of the muscle cell.

The most interesting disclosure of this extraordinary change is that afforded by sections stained first by Weigert's elastic stain, followed by some suitable nuclear and contrast stain. Hematoxylin followed by eosin, or better Van Gieson's mixture, yields satisfactory results,

but by far the most brilliant findings are observed in sections stained with carmalum followed by picric acid. In sections stained for elastica it is found that nearly all that structure designated hyalin in the description of mounts stained by ordinary methods has now elected the elastic tissue stain and stands out as a most striking feature, enabling one even by the unaided eye to designate the areas in which the most conspicuous alteration can be seen. Under the higher powers of the microscope (2.5 mm. homo. im.) the muscle cells of the affected areas are found to be surrounded by a distinct limiting band of extreme thinness—a faint filament—that seems to bind adjacent elements together. In such areas the muscle cells show no conspicuous alteration, the nuclei staining about as the normal, possibly with slightly less intensity, but certainly not in a manner that, in the absence of other lesions, would attract attention. In the areas that, by other methods, previously showed in the most striking way the presence of such reactions as are commonly observed in many infections and usually looked upon as manifestations of hyalin metamorphosis, or coagulation necrosis, the body that previously elected the stains sometimes regarded as characteristic of hyalin now elects to a large degree the Weigert stain. The intercellular spaces immediately surrounding the muscle cells are now occupied by the slaty-black, greatly altered elastica. In the uninvolved muscle complexus the elastica is a most delicate filament, smooth and uniform, lying closely to the adjacent cells; in the altered areas it is coarse, rarely filamentary, but rather nodular, looking like irregularly beaded strings that distend the intercellular spaces. It is evident that the elastica is swollen to two or three times its normal volume, and that in the progress of this swelling the muscle cells have been greatly altered. From the study, so far progressed, it is not possible to say that all the material that appeared hyalin is now shown to be elastica, but certainly an overwhelming preponderance gives a perfectly characteristic elastica reaction. The irregular nodular or beaded appearance would at first appear to be due to a pure sectional view of elastic fibers, but in the immediately adjacent unchanged muscle



the reaction is that of lines surrounding the muscle cells, and only here and there the suggestion that dot-like bodies are really sectional areas of fibers. The possibility that muscle cells are surrounded by an elastic membrane has been considered, but no conclusion is as yet justified by the findings. If such a membrane be present it is reasonable to assume that it must be fenestrated, and hence on section, when greatly swollen, the points of net-like junction would be most conspicuous. The lesion is so located in one of the blocks of tissue examined in this series that it has been possible to serial a complex through over one centimeter, and show that it follows and is largely limited to the complex involved, not extending, in this instance at least, to juxtaposed complexes, although a second complex showing the change was encountered while following out the first observed; the two were not apposed, but both are mesially placed in the muscle layer of the vesical wall.

The ultimate character of the alteration will be discussed in some later communication, in which will be recorded the results of study of the change in this form of muscle in a number of conditions and in the heart, for it has been possible to develop conclusive proof that the heart may be similarly affected.

As regards the peritoneal surface of the bladder the endothelium of the serous layer is for the most part exfoliated. The subserosa is swollen and infiltrated by both cocci and bacilli, and shreddy fragments of necrosing tissue project from the surface; the blood-vessels are intensely engorged and occasionally thrombosed; areas of true rhexis are not abundant. At points in the submucosa other than those mentioned, and in the subserous layer, a few extravascular erythrocytes can be seen, but the sections have failed to catch areas in which the hemorrhage was shown clearly macroscopically. It is probable, however, that the appearance of hemorrhage was exaggerated in the macroscopic specimen by reason of the fact that the masses of necrotic tissue closely resembled distinct areas of hemorrhage. The richness of these structures in bacteria is one of the most conspicuous of the many abnormalities; cocci and bacilli are abundant in nearly all the sections, and so intimately associated that both must have been active simultaneously.

Uterus: Sections from a number of points in the uterus were prepared, but only those will be described that were taken from near the fundus on the anterior surface. In none of the sections so far examined has it been possible to detect the presence of placental tissue.

The conditions found are those of overwhelming infection, as evinced by the abundance of leucocytes, hyalin (?) and necrotic changes in vessels, connective tissue, and muscle, the presence of thrombosed sinuses, etc. The thrombi contain large numbers of bacteria, in some places the bacteria staining with such intensity that the individual elements cannot be made out even in the thinnest sections.

The inner aspect of the organ (uterine cavity) is formed by a hyalin and granular necrotic tissue in which but few cellular elements can be stained; shreds of uterine muscle project into the cavity and are covered and infiltrated by both cocci and bacilli; immediately beneath this necrotic layer is an intensely stained zone containing polymorphonuclear leucocytes, a few hyalin cells, and an abundance of cellular detritus and many bacteria. Sometimes in this zone and sometimes beneath it one recognizes the presence of thrombosed sinuses; the contained thrombi are composed of blood cells, many of which are fragmented, and a small amount of demonstrable fibrin. The margin of these sinuses is formed by walls of leucocytes, many of which are fragmenting, and within the necrosing thrombus innumerable bacteria are variously grouped. In some areas cocci predominate, in others the conspicuous organism is a bacillus possessing the stain reactions and morphology of a member of the colon group. While the thrombosed sinuses are often conspicuous near the inner aspect of the uterine wall, many are more deeply situated. Occasionally smaller vessels and even arteries are thrombosed, and around these one recognizes mantles of polymorphonuclear leucocytes constituting a veritable purulent infiltration of the perivascular tissues. The serous covering of the organ and the superficially placed muscle show practically all the changes already described as present in the bladder. They are possibly less conspicuous, or it may be less advanced.

*Bacteriologic Report.*¹—Specimen consists of agar tubes inoculated from the renal vein, uterus, peritoneum, right ureter, and spleen; and spreads made from the peritoneum.

No growths developed in the tubes from the renal vein and spleen.

The culture from the right ureter contains a bacillus that possesses the morphology and tinctorial reactions of bacilli of the colon group, and a coccus that corresponds to the staphylococcus pyogenes aureus.

From the uterus and peritoneum a pure culture of the same bacillus was obtained.

The spreads contain polymorphonuclear leucocytes, hyalin cells, and what are probably endothelial cells. There is also present an enormous number of bacteria. Some of the bacteria are arranged in irregular zoöglea, so that the individual organisms cannot distinctly be made out. Cocci are seen that correspond morphologically to the ordinary cocci of suppuration. Encapsulated cocci possessing the morphology of the diplococcus of pneumonia are also present. This organism was not obtained in the cultures, and hence its identification must remain doubtful. The spreads also contain intracellular diplococci resembling slightly the gonococcus, but they retain the dye by Gram's method.

Bacilli are also seen, some 2μ to 3μ in length, 0.3μ to 0.4μ in thickness, others 4μ to 5μ in length, with ends slightly clubbed. The bacilli first mentioned occur in pairs, ungrouped and in short filaments, and decolorize by Gram's method. The larger bacilli occur principally ungrouped, possess granules reacting to Neisser's stain, and retain the dye when treated by Gram's method; they resemble the bacillus diphtheriæ morphologically and tinctorially, but were absent from the cultures.

Remarks.—The lesion is undoubtedly one of mixed infection, the conspicuous organisms in the process being (1) the ordinary pyogenic staphylococci; (2) the bacillus coli communis or an allied

¹ I am indebted to Dr. Randle C. Rosenberger, Bacteriologist to the Jefferson Medical College Hospital, for bacteriologic examination and report here incorporated.

member of the colon group; (3) bacilli that morphologically and tinctorially resemble the diphtheria bacillus—the last named are few in number, and were not obtained in culture; (4) diplococcus pneumoniae.

The organisms found were distributed as follows: In spreads, pyogenic staphylococci, diplococcus pneumoniae, bacillus coli communis, bacillus diphtheriae (?).

From the uterus and peritoneum pure cultures of a bacillus of the colon type, although films and sections show that in both situations other organisms were present. In culture from the right ureter a bacillus of the colon group and staphylococcus pyogenes aureus.

The examination of the viscera in this case was restricted to those mentioned, and the report is therefore lacking in fulness. The findings in the tissues examined are those expected in a septic process, and have been given in detail as completing so far as possible the anatomic picture with which the unique changes in the bladder, uterus, and ureteral wall were associated. The detailed study of the structural and microchemic alterations in the bladder wall seems to open a wide field for speculation and investigation. Changes in the muscle of stomach and intestine of the kind here recorded would elucidate many complex clinicopathologic phenomena at present not fully appreciated, *e.g.*, acute dilatation of the viscera named in many conditions—sepsis, peritonitis, inflammations of the mucosae, typhoid fever, etc. The demonstration that, in this case, what appeared on first examination to be a form of hyalin degeneration of a type identical with that described in the heart, vessels, etc., or a form of diffuse coagulation necrosis, was later found to be the result of some change in the elastica, intercellular bridges, etc., suggests the possibility that what has been looked upon as a type of hyalin necrosis when seen in other organs or tissues, on further examination may prove to be the result of alterations in the elastica.

The condition observed in this case resembles closely, if it be not identical with, the described necroses that occur in the heart in various infectious diseases, and should further observation establish

that in infections the unstriped muscle fibers of the body are liable to necrotic, coagulative, or other retrograde changes such as are well known to occur in the heart, we would have a satisfactory explanation of the dilatation of the stomach and intestine, yielding of the arterioles, overdistention of the capillaries, the occurrence of hemorrhage, and many other admittedly confusing problems. The comparatively recent introduction of an acceptable stain for elastica places us in a position to examine anew all those conditions upon which it promises to throw a flood of light; while the observations here recorded do not seem to justify any conclusion as to whether the change is initial in the elastica with secondary wasting and disappearance of the cell, or the reverse, it may be possible by a more extended study of the subject to formulate a definite opinion as to this very important question. The two changes appear so intimately associated in the specimens examined that it seems quite impossible to separate them, and though studied by every method at my command, it has not seemed possible to give either precedence. Sometimes the pericellular elastica may be swollen slightly without conspicuous change in the cell body or nucleus; on the other hand the last named structures may be altered without evident abnormality in the elastica; but the overwhelming evidence is that the two changes occur together.

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LITHIOMERCURIC IODID.

BY

RANDLE C. ROSENBERGER, M.D.,

AND

JOSEPH W. ENGLAND,

of Philadelphia.

From the laboratories of the Jefferson Medical College Hospital.

It has been generally assumed that the active radical of soluble mercuric salts (in their destructive action upon bacteria and bacterial products) is the mercurial, and that the higher the percentage of mercury, the more destructive the compound of bacteria. This theory is apparently confirmed by the fact that the average dose for the human being, of corrosive mercuric chlorid (which contains 74% of combined mercury) is one-half that of mercuric iodid (which contains only 44% of combined mercury). But, on the other hand, it is nullified by the fact that experiments, reported first by Dr. Eugene P. Bernard, of Philadelphia (1886), have shown that mercuric iodid is fully three or four times as powerful in its effects upon bacteria as corrosive mercuric chlorid, indicating that the combined iodine of mercuric iodid is as important a factor in the bactericidal action of the salt as the combined mercury, if not more so.

When used in the form of a germicidal solution, mercuric iodid is dissolved in water with the aid of potassium iodid, producing potassiummercuric iodid. We have found that lithium iodid forms an analogous compound with mercuric iodid, possessing features of superior value. This compound contains, practically, 84% of mercury, 65% of iodine, and 1% of lithium. It is very soluble in water, and has a higher percentage of combined iodine and mercury than the potassium compound, which is due to the lower atomic weight of lithium compared with that of potassium (7:39).

As the solution of lithiommercuric iodid is a much more delicate precipitant of alkaloïds than mercuric chlorid or other soluble mercuric salts, it is reasonable to

believe that, in view of the alkaloidal-like character of the toxins of microorganisms, it decomposes these poisonous principles more effectively than the other mercuric salts. Not being precipitated by fixed alkalies, the solution is not decomposed by the alkalies of the blood or blood-serum. Being a stronger germicide than mercuric salts generally, a less quantity is required to do a given amount of germicidal work; and hence, with its use, there is less danger of mercurial poison.

Bacteriologic tests were made of lithiomericiodid, using solutions of the chemically pure anhydrous salt in a normal salt solution. The results of the several series of tests are given in tabular form. Growth is indicated by +; sterility by —. The experiments were controlled, and in every instance the controls grew luxuriantly.

Staphylococcus pyogenes aureus.

MOIST THREADS. STRENGTH OF SOLUTION.				DRY THREADS. STRENGTH OF SOLUTION.			
Time.	1 : 1000	1 : 5000	1 : 10000	Time.	1 : 1000	1 : 5000	1 : 10000
30 sec...	—	+	+	30 sec...	+	+	+
1 min.	—	—	—	1 min.	—	—	—
2 min.	—	—	—	2 min.	—	—	—
3 min.	—	—	—	3 min.	—	—	—

Streptococcus pyogenes.

MOIST THREADS. STRENGTH OF SOLUTION.				DRY THREADS. STRENGTH OF SOLUTION.			
Time.	1 : 1000	1 : 5000	1 : 10000	Time.	1 : 1000	1 : 5000	1 : 10000
30 sec...	—	+	+	30 sec...	—	—	—
1 min.	—	+	+	1 min.	—	—	—
2 min.	—	—	—	2 min.	—	—	—
3 min.	—	—	—	3 min.	—	—	—

Bacillus pyocyaneus.

MOIST THREADS. STRENGTH OF SOLUTION.				DRY THREADS. STRENGTH OF SOLUTION.			
Time.	1 : 1000	1 : 5000	1 : 10000	Time.	1 : 1000	1 : 5000	1 : 10000
30 sec...	+	+	+	30 sec...	+	+	+
1 min.	+	+	+	1 min.	+	+	+
2 min.	+	+	+	2 min.	+	+	+
3 min.	+	+	+	3 min.	—	+	+

Bacillus coli communis.

MOIST THREADS. STRENGTH OF SOLUTION.				DRY THREADS. STRENGTH OF SOLUTION.			
Time.	1:1000	1:5000	1:10000	Time.	1:1000	1:5000	1:10000
30 sec...	—	+	+	30 sec...	—	+	+
1 min.	—	+	+	1 min.	—	+	+
2 min.	—	—	+	2 min.	—	—	+
3 min.	—	—	+	3 min.	—	—	+

Bacillus anthracis.

MOIST THREADS. STRENGTH OF SOLUTION.				DRY THREADS. STRENGTH OF SOLUTION.			
Time.	1:1000	1:5000	1:10000	Time.	1:1000	1:5000	1:10000
30 sec...	+	+	+	30 sec...	+	+	+
1 min.	+	+	+	1 min.	+	+	+
2 min.	+	+	+	2 min.	+	+	+
3 min.	+	+	+	3 min.	+	+	+

Longer exposures were made in 1:1000 solutions, varying from 5 to 30 minutes. In the moist condition the organism was destroyed in 30 minutes; on the dried threads it was killed in 15 minutes.

As regards the antiseptic or bacterial inhibiting action of the reagent, it was found that a 1 to 16,000 solution readily inhibited the *B. coli*, *B. pyocyaneus*, *B. anthracis* and *Streptococcus pyogenes* for 24 hours.

The next experiment was to determine whether the reagent acted upon organisms in the presence of albumin, as well as in its absence. Solutions were made of the strength of 1 to 1,000, (using equal parts of a sterile normal salt solution and a 5% salt solution of a pleural exudate. The 5% solution of pleural fluid contained 2% of albumin, determined by Esbach's albuminometer.

Threads soaked for 24 hours in 48-hour old cultures of *Streptococcus pyogenes* and *B. anthracis* were used in a moist condition. No growths were demonstrable in 48 hours.

Our conclusions are that in lithiomeric iodid we have a germicide which is very much more powerful than mercuric chlorid or the usual mercuric salts in its destructive action on bacteria and their toxins, and that as it contains less combined mercury, it is, therefore, less liable to cause poisoning on absorption.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD WITH PERNICIOUS ANEMIA.¹

BY WILLIAM PICKETT, A.M., M.D.,

Instructor in Neuropathology and in Psychiatry, Jefferson Medical College; Examiner of the Insane, Philadelphia Hospital.

CLINICAL NOTES.

Lena W——, married, 51 years of age, was admitted to the Jefferson Hospital May 14, 1901.

Family history is negative. In her personal history there is a record of scarlatina at 15 years of age, rather severe, but with complete recovery. Five children are living and healthy.

About two years ago she noticed general weakness, more marked in the legs, with numbness and "crawling" sensation in the legs and feet; this grew progressively worse.

On admission to the hospital there was dyspnea, extreme weakness, pain in the back, and a sensation of a band about the waist; there were involuntary jerking movements of the legs, and pronounced difficulty in walking, so that she fell repeatedly. There seemed to be general visceral ptosis. Urinalysis revealed nothing of interest.

She was examined by Professor Dercum, who found the gait to be both spastic and ataxic, the knee-jerks exaggerated—the right more so than the left; the Babinski reflex pronounced on both sides, the tendon reactions in the arms plus, and all forms of sensation apparently preserved. He found also pretibial tenderness, disappearing ankle clonus, and nystagmus, quite marked laterally and slight vertically. The eyes were examined by Dr. de Schweinitz, who found both media clear; discs oval; arteries carrying very pallid blood; veins greatly distended and pressed upon by the somewhat rigid arteries; no recent hemorrhages, but evidence of previous hemorrhage.

¹ For the privilege of reporting this case I am indebted to Prof. H. A. Hare, into whose wards the patient was admitted, to Dr. Thomas G. Ashton, who had charge of the case, and to Prof. W. M. L. Coplin, through whom the cord came into my hands.

A blood count made three days after admission revealed:

Erythrocytes	1,650,000
Leucocytes	5,400
Hemoglobin	38 per cent.
(Color-index.....)	1.15)

There were large numbers of macrocytes and poikilocytes, a few microcytes, and one megaloblast.

Differential count of leucocytes:

Polymorphonuclear.....	33 per cent.
Small lymphocytes.....	57 per cent.
Large lymphocytes.....	6.5 per cent.
Eosinophiles.....	3 per cent.

Epistaxis occurred on the 21st, one week after admission. A blood count made on that day revealed:

Erythrocytes	1,570,000
Leucocytes.....	7,800
Hemoglobin.....	34 per cent.
(Color index.....)	1.08)

Numerous macrocytes, poikilocytes, four macroblasts, and one microblast were found.

Differential count of leucocytes:

Polymorphonuclear.....	49.5 per cent.
Large lymphocytes.....	3.5 per cent.
Small lymphocytes.....	46.5 per cent.
Eosinophiles.....	.5 per cent.

Ten days before death the patient was found, in the morning, to be completely paraplegic, and the bowels and bladder altogether incontinent, this aggravation of her symptoms having come on in the night. The state of sensation at this juncture and subsequently was not recorded.

For special reasons, only the thoracic and upper lumbar cord was obtainable at the autopsy; and this was put at once into Müller's fluid, no portion being reserved for treatment with special fixatives, although fair results were obtained later with the finer cell-stains in the hands of Professor Coplin. I relied chiefly upon the Weigert-Pal and Marchi methods, and most of the specimen was subjected to these two processes, as well as to those of general staining.

In cross section, after hardening in Müller's fluid, the cord presented, macroscopically, the appearance of "combined sclerosis," and in the Weigert-Pal preparations we see more clearly, on naked-eye inspection, the general picture of "posterolateral sclerosis" which Gowers indicated as the anatomic basis of his ataxic paraplegia.

Under the microscope, at the level of the second thoracic segment (Fig. 1), the Weigert-Pal preparation reveals almost complete disappearance of the medullary sheaths along the dorsomedian septum (Fig. 2) in two-thirds of its extent from the gray commissure, but a relative preservation of them along the dorsal third of the septum, the preserved area having the familiar shape of a flask with flaring mouth at the margin of the cord. Elsewhere in the columns of Goll the degeneration is advanced, but less and less so as the columns of Burdach are approached.

The latter columns, by their comparatively normal state, contrast with the columns of Goll, and at each dorsolateral septum (which in this cord is clearly marked) between the two columns, the transition is even abrupt between the degenerated and the relatively healthy columns. In longitudinal sections the degenerated fibers show the characteristic beaded appearance of their myelin sheaths.

The dorsal root-zones are free of "sclerosis" but show a considerable number of empty spaces, which form a striking histologic feature appearing thus in an otherwise dark-stained field.

Lissauer's zone and the dorsal roots are normal.

The lateral columns are quite symmetrically degenerated. The affected zone on either side is of oval shape and is nearly confined to the crossed pyramidal tract, but reaches the surface of the cord in the midst of the direct cerebellar tract, which has thus lost a crescentic portion of its cross area. The direct cerebellar tract mainly, however, is uninvolved. The degeneration in the lateral column is nowhere so extreme as that in the columns of Goll, but empty spaces are a more marked feature, particularly at the periphery of the crossed pyramidal tract, and many of these empty spaces are found throughout the "lateral ground" area.

Ventrally there is an aggregation of empty spaces in the region of the direct pyramidal tracts, which are thus mapped out by a sieve appearance (Fig. 3). Dr. Coplin has pointed out in my sections the persistence of the supporting neuroglia in these vacuoles, as a dim network whose meshes correspond to nerve fibers which have disappeared.

Van Gieson's mixture and other general stains show an overgrowth of neuroglia which varies in density from the complete sclerosis of the middle zone (septal) of the dorsal region, to a slight trace of it on one side of the ventral sulcus. Sections treated with Weigert's neuroglia stain by Dr. Coplin reveal this feature very clearly.

Toluidin blue, Nissl's methylene blue, Delafield's hematoxylin, etc., fail to bring out any changes in the ganglion cells. The walls of blood-vessels are perhaps somewhat thickened, but the change is not confined to any region or tract of the cord. The central canal is somewhat dilated throughout.

At successively lower levels of the cord similar changes are found, the "combined degeneration" being as clearly marked at the lumbothoracic junction as at the second cervical segment; but there are two important differences with respect to the distribution of degenerated fibers in the lowermost sections (Fig. 4); (1) the sclerosis is somewhat evenly spread over the dorsal columns—not concentrated in the columns of Goll, nor more pronounced along the middle line, but extending through the column of Burdach, save for a narrow strip of the root-zone; (2) the crossed pyramidal tract is more sharply cut out by the lesion. Empty spaces in the areas near the crossed pyramidal tract, in the direct pyramidal tract, and in the root-zones are marked as at higher levels.

The columns of Clarke, wherever found, are well developed.

Marchi preparations from different levels show the black masses distributed rather widely, but far more abundantly in the dorsal columns and crossed pyramidal tracts than elsewhere. Where the sclerosis is most marked there the osmic stained masses are thickly sown (Fig. 5); and there is no separate zone of this broken-down myelin beyond the line of empty spaces, such as Russell, Batten and

Collier, and Putnam and Taylor describe. In other words, from my preparations it would appear that degeneration, represented by (1) broken-down myelin (Marchi), and (2) neuroglia-sclerosis, has implicated the long tracts (pyramidal, Goll and Burdach), while that represented by empty spaces has spread irregularly but for the most part laterally. It is conceivable that this last process was the cause of the final complete paraplegia, as it probably is indicative of a process of very recent origin.

That some of the efferent fibres entering at the root-zone trend toward the middle line as they ascend the dorsal columns is well known; and hence that a sclerosis of these columns widespread in the lumbar cord should be concentrated along the dorsomedian septum at the cervicothoracic junction is a feature of tract degenerations, just as the growing sharpness of outline of the pyramidal tract degeneration from above downward belongs to system diseases. At any rate the process is partly systematic, so that the term "diffuse" applied to this subacute combined degeneration by Putnam and Taylor is not adequate for this case, as it is not for Case V of their own series, in my judgment. Some such term as *para*-systematic might be useful here.

Westphal described combined system disease of the spinal cord in 1879; Gowers's classic lecture on ataxic paraplegia appeared in 1885; and probably in the conception of each of these authorities were embraced cases like the present one. Before those years, and even later, it was customary for the Germans (Strümpell) to apply the term "tabes" to these cases of dorsolateral degeneration as well as to cases of tabes dorsalis. Accordingly when Leichtenstern in 1884 described two cases of tabes (with increased knee-jerks) as running the course of pernicious anemia, he apparently hit upon the very type which is attracting attention to-day. Two years later Lichtheim studied the cord changes of pernicious anemia so thoroughly that subsequent workers have made comparatively little advance in the direct elucidation of the lesion, and to Lichtheim has been accorded the credit of priority. Many papers confirmatory of Lichtheim's findings have appeared; among the earliest being those of Putnam, Dana, Nonne, and Charles W. Burr.

The striking histologic features of the cord lesion—empty spaces in the white matter, and rather slight “sclerosis” in the degenerated areas—were described by Lichtheim; but while subsequent writers have found these features almost constant, some of these changes, notably empty spaces, have been discovered in early tabes dorsalis, and they probably represent a *subacute* phase of the ordinary parenchymatous degeneration of nerve tissue.

To Putnam and Taylor we owe a demonstration and a hypothesis. The demonstration is, that an unbroken series exists, both clinically and pathologically, from the cases of Lichtheim, Burr, etc., to cases of Gowers's ataxic paraplegia—pernicious anemia being associated with a few of them. The hypothesis is that in this entire series a toxemia, ranging in its manifestations from slight cachexia to pernicious anemia, is the causative factor.

The Italian Bastianelli, discerning independently these two series, (1) of spinal cord manifestations, (2) of blood manifestations, has imagined an inverse relationship between them which we might represent diagrammatically thus:

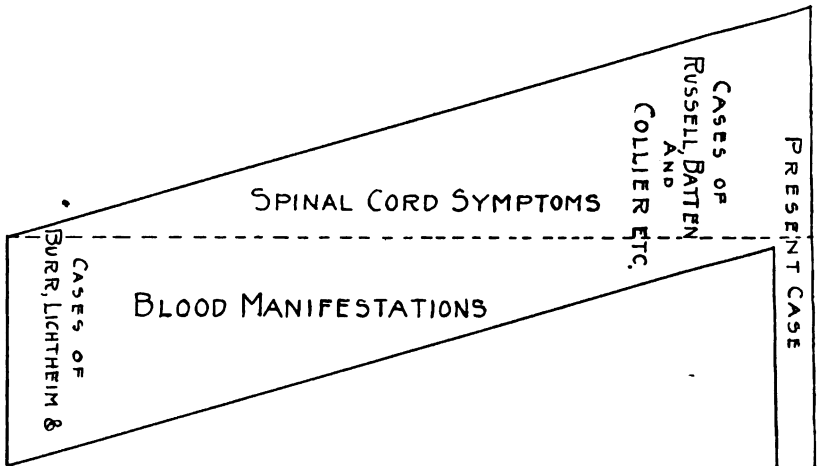


DIAGRAM NO. I.

Why there should be this inverse relationship is difficult to see; and in fact it does not hold for cases like the present one, in



FIG. 1.—Cord, upper thoracic (for description see text). Weigert-Pal stain. Magnified nearly 6 diameters.



FIG. 2.—Cord, upper thoracic (same as Fig. 1; for description see text). Magnified 13.3 diameters.



FIG. 3.—Cord, upper thoracic (same as Fig. 1; for description see text). Magnified 13.3 diameters.

which the blood state and the cord symptoms are both extreme, nor for Case V of Putnam and Taylor's series, as pointed out by Taylor.

Russell, Batten, and Collier, in an authoritative paper, conceive of a relationship between the anemia and the cord symptoms which modifies our diagram to something like this:

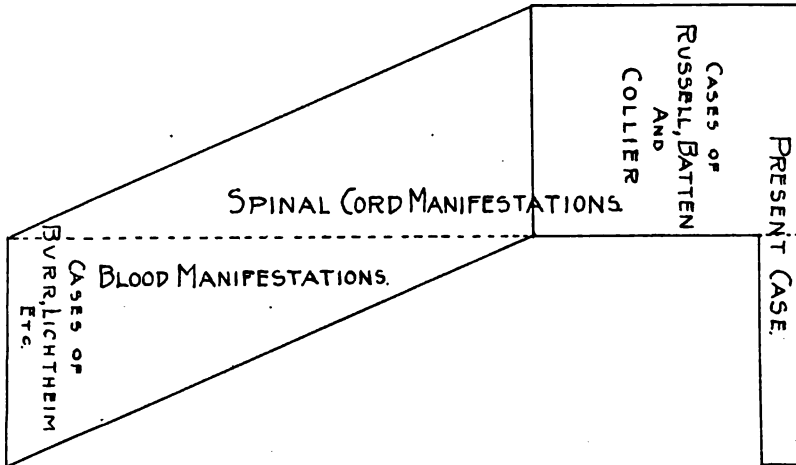


DIAGRAM NO. 2.

for they say, speaking of the cases with severe anemia, "in none of them have there been, either clinically or after death, the phenomena which characterize the class of case whose pathology we are now considering," and which these authors regard as a distinct nosological entity.

But here again our present case opposes itself to a rather premature generalization, for in its clinical course it allies itself with Russell's type, as it does with respect to the cord lesions found, though associated with pernicious anemia.

To support the hypothesis of a toxemic origin of this wide series of cases, Putnam and Taylor have marshalled an array of clinical data—diarrhea, constipation, "lack of vigor," various stigmata of degeneration, etc.—which are so common in the medical history

of sick people generally that they are not convincing. Historically it would appear that the very origin of the toxemia theory was the discovery of the coincidence of severe anemia and cord degeneration, and we think such coincidence as in the present case is still the strongest support for that theory. Deprived of this support, as it is seen to be in the conception of Russell, Batten and Collier, from the quotation above, "toxemia" becomes as vague and sterile as it is in some of its other uses, or as "degeneration" has become in psychiatry.

A suggestive observation was made by Nonne, and has been confirmed by a number of others, as to the mechanism of the peculiar cord degeneration in these cases. Hyaline degeneration and thickening of the walls of vessels, particularly of the capillaries, had been found by several observers in a considerable proportion of the cases, but Nonne, constructing out of his cases a series, graded from those in which cord changes were barely discernible to those showing the familiar wide-spread column degeneration, essayed to demonstrate that the slighter patchy degeneration in cases at the one end of his series was distributed around diseased vessels, presumably by the mechanism of a local anemia from diminished carrying power of these vessels; and assuming a homology between this *series of variations* of the cord lesion and a *series of stages* in individual cases, Nonne concludes that degeneration in all cases begins in patches corresponding to the *district of supply* of individual diseased vessels, that the more widespread areas in pronounced cases result from the coalescence of these patches, and that hence vascular disease is primarily concerned in the quasi-systematic cord diseases of pernicious anemia.

Whatever may be said of this process of reasoning, we may assume that such regional differences in the state of vessels, while more obvious in early cases, would still be apparent even in advanced stages of the cord disease, so that it is a question of fact to be investigated in every case that comes to hand. Russell, Batten, and Collier did find the diseased vessels in the degenerated areas only; but Spiller, in his report of a case (Hughes and Spiller), declares that the hyalin vessels were scattered and seemed to have no rela-

tion to degenerated areas; and the same is true of our case. Nonne regards such "negative" evidence as of slight import when weighed against his positive findings; but on the contrary we may suggest that if local vessel disease be the important factor, it must be always present, and since on the authority of Spiller and others it is to be declared inconstant, there must be another solution of the problem.

Indeed, in considering the sequence of changes according to Nonne's view—(1) toxemia, (2) discriminative vessel disease, (3) corresponding areas of degeneration—it appears *a priori* just as easy to explain why the last should be discriminative; and conversely, just as difficult to account for the selection of certain vessels in the process as to account for the selection of the corresponding areas of the cord. In either case we are obliged to recur to the well-known doctrine of Marie, which accounts for the involvement of the dorso-lateral white matter at all levels by postulating a less copious supply of blood in those sectors of the cord's circumference than in the ventrolateral sectors, these two portions being supplied by separate sets of vessels. Yet even here we are confronted with a paradox, pointed out by Russell, Batten and Collier, in that the cervical and upper thoracic regions of the cord, which are the favorite seat of this degeneration, are in truth more abundantly supplied with blood than the lower levels, which are commonly only slightly involved in the disease.

However, by any simple theory of ischemia, or of local toxemia, we might expect to find the degeneration more *sector-like* than we do in most cases; in all cases there is some approach to the system picture of degeneration. As Spiller has expressed it "they appear to the naked eye to be system degenerations." Some time ago in attempting to demonstrate the comma fields of Schultze, the oval field of Flechsig, etc., in a cord from a typical case of tabes dorsalis secured at the Philadelphia Hospital for teaching purposes, I was disappointed to find these so-called endogenous tracts completely degenerated and indistinguishable. This is not unusual, and I mention it merely for the suggestion it contains, that we must not be too stringent in our requirements of what shall constitute a system disease, lest we put the whole subject into confusion.

That seems, therefore, a wise conclusion reached by Putnam in 1891, but later abandoned by him, and newly insisted upon by Russell, that in these cases of subacute combined degeneration of the cord we have to do with two processes, one systematic, the other diffuse.

The present case is recorded for the support it lends to that conclusion; and as a slight rebuttal of the view that the subacute combined degeneration of Russell, Batten and Collier is never associated with pernicious anemia.

POLYHYDRAMNIOS; ITS DIFFERENTIAL DIAGNOSIS AND TREATMENT, WITH THE REPORT OF CASES.

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The following cases, occurring recently, illustrate the clinical history, diagnosis and treatment of this condition:

CASE 1.—Seen in consultation with Dr. Loeb. A multipara, aged 40. Mother died of heart disease, father of dysentery. She had born a number of children without dystocia; gave no history of puerperal septic infection, but stated that during the present pregnancy her appetite had been poor and she had suffered much from enlargement of the abdomen, dyspnea and inability to sleep. On examination, the abdomen was greatly distended, fetal heart sounds could not be heard, ballottement could not be obtained, no presenting part could be felt, but by palpation a hard body could be indistinctly outlined within the womb. The patient was admitted to the Jefferson Maternity. Her dyspnea increased so rapidly and her general condition was so poor that interference was imperative.

On examination, the internal os was tightly closed. Under antiseptic precautions, McLean's bag was introduced into the cervix, but two hours after its introduction the patient pulled it out, causing a tear in the cervix, from which considerable blood was lost. An hour afterward the patient's condition demanded that the uterus be emptied as speedily as was safe. She was accordingly placed upon a table, a broad bandage held across the abdomen by assistants, who pulled downward and backward upon the bandage, making continuous and firm pressure. The membranes were then ruptured and eleven quarts of amniotic fluid gradually escaped, the fingers plugging up the cervix to prevent the rapid flow of fluid. As the fluid escaped, the pressure upon the abdomen was increased, the fetus turned transversely and was delivered by podalic version. The patient was controlled by partial anesthesia, the placenta removed, the uterus thoroughly douched with

creolin 1% and packed with iodoform gauze. The patient received one pint of saline fluid by intravenous transfusion. Strychnine and ergot were given freely and the patient rallied well from the delivery. A large pad was placed above the uterus and the abdomen was firmly bandaged by a many-tailed abdominal binder. The patient made an uninterrupted recovery.

Although the fetus moved after birth, it did not breathe. Its cranium was abnormally shaped, the occipital bone having completely developed, while other portions of the cranium were markedly deficient. Upon autopsy the thoracic and abdominal viscera were normal. A small quantity of unorganized gray matter took the place of the brain. No cerebrum was present. The spinal cord was rudimentary in development, its membranous covering being absent.

CASE 2.—Multipara, aged 31, was sent to the Jefferson Hospital for the removal of a cystic tumor and referred to me at the the Maternity. The patient's father died of phthisis. She had had seven children: the first was delivered by forceps, the others spontaneously. During previous pregnancies, her general health had been excellent; she had no nausea and could do her housework during the entire time. During the present pregnancy, her general health had been excessively poor. Early in pregnancy she had much nausea, and lately the abdomen had enlarged so rapidly that she could not lie down, and suffered greatly from dyspnea. She menstruated last in October, and was 5 months advanced in pregnancy. The abdomen had been larger than normal throughout the entire pregnancy, but distension had been especially rapid for the last six or eight weeks. Urine: deep amber, specific gravity, 1028; acid; urea, 1.8%; no microscopical debris. Blood: Red bloodcells, 4,500,000; white cells, 4,800; hemoglobin, 65%; color index, .68.

On examination, the abdomen was uniformly enlarged, the distension being so great as to embarrass respiration seriously. Over the center of the abdomen dulness was heard upon percussion with moderate tympany over the transverse, ascending and descending colon. No fetal parts could be felt by palpation, nor could heart sounds be heard. The thoracic organs were normal, with the exception of a few rales over the bronchial tubes and a disturbed action of the heart. Upon vaginal examination the pelvic floor was elastic and the cervix had been lacerated in former labors. The finger could be readily carried through the cervix and against the membranes, which were not tense. A body giving the sensation of a small fetal head dropped against the finger upon introduction, and ballottement could be very distinctly obtained with an appreciable interval of time between the first and second impact of the presenting part. A diagnosis of rapidly increasing polyhy-

dramnios was made and the patient readily agreed to the termination of pregnancy.

The patient was antiseptically prepared for operation, and the membranes were ruptured at 12.40 P. M. on the following day. About 2 gallons of fluid were allowed to escape gradually, when the presenting part was allowed to come against the cervix to check the flow of fluid. Compression was made over the abdomen during the removal of the fluid, and a many-tailed abdominal binder was afterward applied. Labor pains soon followed the removal of the fluid, at about 3 o'clock a male child was expelled, and 10 minutes later a second male fetus within its amniotic sac. There was one chorion, but two amnions. Both cords were attached to the same placenta, which was abnormally large, very thick and with its tissues in a condition of apparent coagulation. The cord of the first child born was remarkable for large and tortuous veins, while its jelly was granular in appearance with areas of cystic degeneration. This cord had a lateral attachment to the placenta, 20 centimeters distant from the attachment of the other cord. The entire specimen was at once sent to the pathological laboratory of the Jefferson College, where complete examination of the specimen was made as follows:

PATHOLOGICAL REPORT.—Placenta and two male fetuses.

There is a single ovoidal placenta which, when spread out, measures 29x18 cm. The end to which the larger fetus is attached is somewhat the larger; the cord of the larger fetus possesses a marginal attachment; that of the smaller fetus is 2 cm. from the free margin of the placenta. The placenta on the side of the larger fetus has a maximum thickness of 2 cm. and is on the whole thicker as well as larger than the opposite end.

The amnion surrounding the larger fetus is evidently much thickened and quite opaque. The opacity is not uniform, but at no point is the membrane so clear or thin as the amnion covering the smaller fetus. While the membrane is, as a whole, thicker and more opaque, the opacity shows a notable intensification in two ways: (1) There is a mottling or flecking formed by rather whitish or grayish white dots, for the most part 2 to 5 mm. in diameter, although a few are larger. These dots are quite opaque in their centers but at the margins fade off more or less gradually to the opacity of the remainder of the membrane. (2) In addition to the flecked opacity there is an equally marked, though less abundant, striation by rather regular bands that interlace in different directions, forming a sort of net-work. These bands vary in width from 1 to 4 or 5 mm. Many of these bands run in a more or less tortuous manner and at the ends either gradually thinned and were lost or split into branches that united with other similar branches or merged into the membrane.

The amnion of the smaller fetus showed nothing noteworthy.

The larger fetus, the amniotic sac of which is abnormal, measures 30 cm. in length and weighs 550 gm. The umbilical cord is 29 cm. in length, irregular in its contour, being bossed or tuberos as a result of lateral acculations. The jelly is unusually translucent and the contained vessels can be seen throughout the major part of the cord. The vessels are dark, extremely tortuous and irregularly dilated.

The cord is much thicker than the cord of the other fetus, possessing a transverse diameter that varies between one and two cm.

The smaller fetus is 27 cm. in length and weighs 395 gm. It is very much more cyanosed than the other; the cord possesses a maximum transverse diameter of 0.6 cm. There is very little twisting of the cord and it seems flat. It is not nearly so translucent as the other and the vessels are not tortuous.

Both fetuses were examined with care, but no visceral abnormality could be detected. The serous cavities of the larger fetus contained possibly a little more fluid than normal, certainly more than the same cavities in the smaller fetus, and there was a suggestion of subcutaneous edema, but it was not marked. A careful examination failed to disclose any gross lesion involving the vascular system of either fetus.

Blocks from a number of points in the placenta, parts of both cords and both amnions, were fixed in Bensley's solution, washed in water, dehydrated, infiltrated, sectioned and the sections stained by approved laboratory methods.

Histology: Cord of the smaller fetus on transverse section was at some points but a thin band, in other sections ovoidal and in still others stellate, having three points in each of which was a vessel; the star-like points were rounded and measured from 1.5 to 2 mm. in width.

Microscopically the cord was surrounded completely by the layers of the amnion. The ectodermal cells were very distinct and clear and several layers were present. The basement layer consisted of small cuboidal cells that took the stain more deeply than those of the upper layers. The cells of the upper layers were comparatively large and polygonal in shape. The nuclei in all stained well and were large and prominent. The tissue immediately beneath the cells was denser than that nearer the center. Just beneath this dense layer were small masses that took the eosin quite deeply. These formed an irregular area almost around the cord. They were apparently bundles of fibrous connective tissue extending longitudinally. No nuclei were visible in these areas.

The middle of the cord consisted of both embryonic and

fully developed connective tissue. The latter seemed to predominate and was prominent, especially in the neighborhood of the vessels. Between these and the periphery the cells were more stellate in type though not of the youngest form. The intercellular spaces were almost entirely filled with a hyaline, faintly acidophilic substance quite free from granules.

The vessels were well developed. The umbilical vein and one artery contained clotted blood. The other artery was free from cells. The stromal tissue was condensed around the periphery of the vessels forming an adventitia. The cells of this tissue were spindle-shaped. The involuntary muscle fibers of the media were well developed; in one of the arteries the media was clearly in excess. In this vessel the intima was greatly thickened, the thickening being more conspicuous on one side than the other, leading to the appearance of nodular thickening of the structure. The extra laminae were of coarsely fibrillated tissue, containing but few cellular elements. Stains for elastica yielded no satisfactory reaction. The wall of the vein did not show, in any of the sections examined, any noteworthy abnormality.

Besides these openings a fourth was noted. This was slit-like—on transverse section, resembling an exclamation point—situated midway between the two arteries, and had neither muscular nor adventitial coat, although the surrounding tissue was somewhat condensed. The lining consisted of 2 or 3 layers of squamous cells. This opening was not present in all sections, and apparently occurs here and there in the cord and is not a continuous cavity.

Cord of the larger fetus: After fixation this cord at the point sectioned was 1 cm. in its long diameter and 0.8 cm. in the other. The ectodermal cells covering the cord were flatter, smaller and less distinct than in the previous cord, and the stromal tissue not far advanced in development. There was little fully developed connective tissue even in the region of the vessels. Neither was there an adventitia as in the above cord. The stellate cells were large and quite numerous and possessed many processes and, although there was considerable intercellular substance, the intercellular spaces were numerous and quite large. They were especially well marked towards the periphery. The stellate cells seemed to be younger than those of the previous section. On the whole, the appearance outside of the vessels was very much like an irregular network. Some spaces were exceedingly large and appeared as though they might have been distended by some fluid, the picture being that of an extremely edematous myxomatous tissue.

One artery and the vein showed no abnormality. The remaining artery showed a notable thickening of the intima.

nodular in character similar to, but more marked than, that already described in the other cord. Near to the abnormal artery and between this structure and the vein was a small group of cells apparently identical with those covering the cord; the outer cells of this group were somewhat flattened and concentrically arranged, while those occupying the center were irregularly grouped. The appearance was suggestive of that resulting from incomplete closure of a canal.

The amnion of the larger fetus was opaque and unusually thick. Microscopically on surface view, it showed thick bands of tissue running in various directions. These bands were quite dense and contained many rodshaped and oval nuclei, many of these resembling those of nonstriated muscle fiber. They were not noticed in slides of the normal amnion. Between these bands the spaces were filled with cells large and small that took the stain fairly well. These cells varied considerably in size and showed a granular protoplasm. They were projected upon the bands also. The tissue between the cells took the stains lightly and seemed finely granular and nearly homogeneous.

Upon section the membrane showed a covering of large irregular cells (ectodermal) arranged in several layers. At some points but two layers of these cells were present, while in other areas irregularly piled cells without lamination were grouped on the surface of the membrane. From their grouping and number it is reasonable to assume that the flecking observed in the gross specimen was due to the accumulation of cells here mentioned. The nuclei of these cells showed prominently and the protoplasm stained but faintly. The nuclei were granular and were, no doubt, the structures described as cells in the description of the surface view of the amnion. The cell margin was not clearly visible either on surface view or on section. The tissue beneath appeared easily separable into layers and in these the nuclei were abundant and prominent; they were rodshaped, oval or round. In the bands already referred to the resemblance to involuntary muscle fibers was pronounced. The specimens studied seemed to be chiefly sections of the dense bands. On the side opposite to the ectodermal cells was noted a single layer of flat squamous cells. The nuclei were darkly stained and distinct, slender and on section rodshaped in structure. They were smaller than the nuclei in the middle part of the membrane.

The placenta was for the most part apparently normal. Sections from a number of points showed no abnormality except that on the fetal surface there was a massing of cells quite like that described as present on the cord. In the superficial part of the chorion above the villi one occasionally observed groups of lymphoid cells sometimes alone and at other points mixed with larger cell elements resembling

those of the syncytium. Some of the arteries near the area of cord implantation showed obliterate changes similar to those already described as present in the diseased trunks. The villi were well developed and the intervillous spaces filled with blood. The cells covering the villi as well as the villous matrix were apparently normal.

The mother made an uninterrupted recovery.

CASE 3.—A primipara was seen at the request of her physician who was ill. There was a family history of tuberculosis, and the patient was not an especially strong woman, but had been better than usual in general health during her pregnancy. Between the second and third months of gestation, she had been greatly frightened by a lightning-stroke which injured property very near her dwelling. She had completed nine months of gestation, and had been much annoyed by pressure symptoms on the right side and in the right thigh. She thought that the child had recently descended low in the pelvis.

On examination her pelvis was of average size. The fundus of the uterus was a hand's breadth above the umbilicus, the tissues above the uterus were much distended, the back of the fetus was upon the left side, its heart sounds left anterior at the pelvic brim and not loud. The head could not be distinctly made out by palpation. On vaginal examination the cervix was very little dilated and but little shortened. A small presenting part (the head) was at the pelvic brim scarcely engaged. The patient had very slight and annoying intermittent uterine contractions, but no positive labor pains. She was given bromides to secure sleep. On the following day, regular uterine contractions occurred with slow dilatation, a small presenting part remaining high up and movable. The amniotic liquid was evidently in excess. When the membranes ruptured, the fetal head at once descended to the pelvic floor, where progress ceased. As the patient was highly nervous, and becoming exhausted, she was delivered by forceps under ether. When the head was born, on inserting the finger to feel for the umbilical cord, the finger passed into the spinal canal through an opening in the lower cervical and upper dorsal region. The child, a male, weighing $5\frac{1}{2}$ pounds, was readily extracted. It breathed feebly, and lived about 10 minutes. While the cranium, although small in size, was well formed, the arches of the vertebræ were lacking in the lower cervical and upper dorsal regions and a meningocele was present. The child was otherwise well developed. The placenta was removed entire by hand, was larger and thicker than it should have been in proportion to the size of the child, but presented no evident anomaly in its vessels. The cord was excessively long and wound in a perfect spiral from left to right. A slight laceration of the pelvic floor and perineum was immediately closed. Precautions were taken to prevent hemorrhage by the use of

a hot intra-uterine lysol douche, followed by packing with iodoform gauze. The patient was stimulated freely and made an uninterrupted recovery.

Upon inquiry no history could be obtained of the occurrence of malformation or deformity in either the family of the patient or that of her husband. The fright in the early portion of pregnancy was the only abnormality which could be found in the case.

CASE 4.—Primipara, white, aged 18. Mother died in confinement, and cause not stated. Pelvis narrowed at the lower portion, expanded at the brim symmetrically; the urine normal, the patient fairly well nourished and suffered little during pregnancy. Complained of pain in the right upper portion of the abdomen, dyspnea and sleeplessness. On examination, abdominal distension marked, fetus could not be outlined, nor could fetal heart sounds be distinctly heard; the patient's lower limbs were considerably swollen, her heart action labored. The patient complained of indefinite pains for several days, when the os was found fully dilated. The patient was given tincture of nux vomica and ergot, the membranes were ruptured and compression applied to the abdomen. When the membranes ruptured, the head immediately engaged, the child descended, and was allowed to emerge from the body of the mother gradually.

The placenta was removed, the uterus douched and packed with gauze. The mother made an uninterrupted recovery. The fetus gasped, but did not breathe; its heart beat persisted for three-quarters of an hour, in spite of respiratory failure. Upon autopsy, general dropsy was found, and in the abdomen and pericardium a large quantity of fluid. The lungs were edematous, the kidneys showed atrophy of the pyramids and the liver was softened and enlarged. The cord was shorter than the average, the placenta boggy, light in color, large and friable. The decidua was much roughened, resembling a fibrinous exudate.

CASE 5.—Multipara, with moderate quantity of fluid. Dilatation well advanced, but pains inefficient because of overdistension of the uterus. Made patient sit on a bucket, punctured membranes and allowed several quarts of fluid to escape. Gave quinine and ergot. The child was speedily delivered; it failed to nourish properly, and died in ten days with symptoms of intestinal obstruction.

The literature upon the pathology of hydramnios is so extensive that it permits but brief reference to the most recent. By hydramnios or polyhydramnios is meant the presence of more than two pints of amniotic liquid at full term. This quantity may be as large as seven gallons in a human species. In an

animal 135 liters have been present. We know little regarding the composition of the amniotic liquid. Certain drugs have been found in this liquid, sugar is occasionally present, the quantity of urea contained in it varies; in some cases it is stained by meconium, while in other cases it contains abundant leukocytes and may even resemble diluted pus.

The pathology of hydramnios still awaits complete explanation. The old statement of Guillemet (*Thèse Paris*, 1876), that hydramnios has no pathological anatomy, is largely true. No constant changes attend this condition. The placenta may be larger than usual, boggy, dropsical and infiltrated. In case two, the vasa propria beneath the amnion were distinctly enlarged, to which attention has been called by Jungbluth (*Archiv für Gynäkologie*, Band 4, page 554, 1872). The amnion and chorion may be thickened or may not be altered. Viti (Bull. de Soc. tra. i cult. d. sc. med. in Siena, III, 196-200; 225-228, 1885) found the epithelial layer of the amnion intersected by large fissures, and subepithelial fibers freely exposed, the protoplasm of the cells granulated, with fatty degeneration. He experimented upon the passage of fluids through the arteries and veins into the placenta by injecting different fluids, and found that seven times the quantity of fluid escaped through the veins that escaped through the arteries. Any fetal condition causing venous engorgement tends to produce polyhydramnios, and this condition, so far as the fetus is concerned, has been likened to the dropsy of adult life caused by disease of the heart or liver. In some cases the formation of irritating (lymphagogue) substances causes polyhydramnios, as shown by Opitz (*Centralblatt für Gynäkologie*, p. 553, 1898)

A natural theory has been that the liquor amnii is fetal urine and that polyhydramnios indicates increased renal action, but in some cases the kidneys show no lesions, the urethra may be occluded or absent, and even

the kidneys may be absent and still polyhydramnios be present. Bar (*Thèse Paris*, 1881) has well stated the older theories, none of which explain all of the phenomena present. Case three of this paper illustrates one theory for polyhydramnios, that the fluid is an excessive secretion from the cerebrospinal canal of the fetus. In this case, the open canal and meningocele give strength to this supposition. Where polyhydramnios follows a blow or fall, flaky deposits are sometimes seen on the surface of the amnion and have been supposed to result from the traumatism preceding labor. It seems reasonable to suppose that lymph can pass freely through the stomata of the amnion. In twins, one fetal sac may contain excessive fluid while the other does not, as was seen in case two of this paper.

While we may not explain adequately by one theory the occurrence of polyhydramnios, we may remember, as Ballantyne (*Manual of Antenatal Pathology*, 1902) has stated, that the relative conditions existing in polyhydramnios are those normally occurring in early fetal life. At the fourth month of gestation, the amniotic liquid weighs more than the fetus or the placenta and membranes. Through conditions which affect embryonal and fetal development this early relationship between the fetus and its hydrosphere continues after the fifth month. It is observed clinically that acute polyhydramnios begins at about the fifth month of gestation.

We may look to pathological chemistry for further knowledge upon this subject. By cryoscopy Resinelli (*Annali di Ostetrica e Ginecologia*, No. 23, p. 1029, 1901) has investigated the osmotic pressure of the maternal and fetal blood and of the liquor amnii by taking the differential of their freezing-points. This pressure is less in the maternal and fetal blood at birth than in the nonpregnant adult, and it is constantly less in the liquor amnii than in the maternal or fetal blood. In twin pregnancies the freezing point of the liquor amnii of one fetus may differ from that of the other. Polyhydramnios is one of

many conditions for which bacteriology presents no solution, but which requires increased knowledge of physiological and pathological chemistry.

The diagnosis of polyhydramnios is important and at times difficult. If the amniotic liquid is accumulating but slowly, haste is not imperative, and in mild cases it may not be necessary to interfere, but if the fluid is increasing rapidly and the patient's general health and comfort are suffering, pregnancy must terminate. The diagnosis of pregnancy is made difficult by the fact that fetal heart sounds cannot be appreciated in advanced cases, nor can the body of the fetus be felt. Pregnancy must be diagnosticated by the changes in the mammary glands and from the history rather than from the usual and positive signs of gestation.

The differential diagnosis between polyhydramnios and abdominal dropsy may be made as follows: In abdominal dropsy, the abdomen is flattened and distended laterally, its dull area changing with the position of the patient. There is no evidence of intermittent uterine contractions, which can often be elicited in cases of polyhydramnios. In abdominal dropsy there is often some cause, as disease of the heart or liver or kidneys, to account for the effusion.

The differential diagnosis between ectopic gestation and polyhydramnios is made by the excessive distention which is not present in ectopic gestation, by the absence of the characteristic pain and shock which are observed in ectopic gestation, and by the history of the case. It must, however, be remembered that ectopic gestation may be complicated by polyhydramnios in its early stages.

In the case of an ovarian cyst there is usually a history of longer illness, the swelling having been unilateral at first. The intermittent hardening in the abdominal tumor is absent and careful bimanual examination reveals the uterus but little enlarged at one side of the tumor. Encysted dropsy or localized

tubercular peritonitis might be impossible of differential diagnosis from polyhydramnios.

When the fact of pregnancy is made out, there comes the second diagnosis between pregnancy and polyhydramnios, or pregnancy and ascites, ovarian cyst, plural pregnancy, an hydatid mole, a very large child or a malformed fetus. In the hydatid mole, the pear-shaped uterus has little fluctuation and there is a history of repeated discharge of blood. In the presence of a large fetus or large and malformed fetus the heart can usually be found, fluctuation and ballottement are absent and careful palpation will reveal the child. Palpation and auscultation will usually give warning of twin pregnancy, and yet, after the most careful examination, twin-pregnancy may be mistaken for polyhydramnios, or the contrary be true. When an ovarian cyst complicates pregnancy, it will be difficult to outline two tumors, and sometimes a positive diagnosis cannot be made. Ectopic gestation must always be kept in mind as a complicating element in these cases.

When polyhydramnios is associated with twin-pregnancy or with ascites, or with an ovarian cyst, or occurs in an ectopic gestation sac, it is often impossible to make a positive diagnosis. When labor begins and the cervix dilates, a diagnosis may be established.

In these and other cases two points have been noticed which are anomalous and without satisfactory explanation. One would naturally expect in the presence of a large quantity of amniotic liquid that the tension of the liquid within the bag of waters would be considerably increased and that the membranes would feel tense when the finger was placed against them. We have not found this to be the case, but, on the contrary, that the membranes remain relaxed and that the amniotic liquid had apparently very little tension, although the quantity of fluid might be large. Under these conditions, one would also expect shortening of the cervix and premature obliteration of the cervix; on the con-

trary, in our observation this does not occur until active labor actually begins. These conditions are misleading and sometimes throw doubt upon the diagnosis.

The treatment of polyhydramnios by the administration of drugs is without known value.

When the quantity of fluid is but slightly in excess and is not increasing rapidly, and the patient's general health remains good, the condition need not be interrupted. In the presence of rapidly increasing distention with large quantity of fluid and interference with the patient's general condition, pregnancy must be terminated. This must be done under thorough antisepsis by dilating the cervix sufficiently to introduce the finger, by puncturing the membranes and allowing a portion of the contained fluid to escape. In allowing fluid to escape, care must be taken to use the fetus as a valve preventing the immediate removal of the fluid. It is usually unnecessary to employ an anesthetic for the rupture of the membranes. The patient is put in an available position, one or two fingers inserted within the cervix, and the membranes are separated from the wall of the uterus as far as possible. Under the guidance of the finger, a pair of closed uterine dressing forceps is gently thrust into the sac and the blades opened sufficiently to permit the introduction of the finger. A portion of the fluid is allowed to escape gradually, the finger acting as a plug until the operator feels the presenting part closing firmly down against the cervix. Then the finger is removed and the amniotic liquid allowed to drain very slowly. The maintenance of firm pressure over the abdomen is most valuable in these cases. Not only is the uterus made to contract, but the patient is saved the severe shock which is often seen when a large body is removed from the abdomen suddenly. Pressure may be applied by a many-tailed abdominal binder, pinned securely, or during the escape of the fluid by a bandage placed across the abdomen and drawn inward by two assistants. With the lat-

ter, pressure can be varied in accordance with the needs of the case. After a part of the fluid has been removed, the patient must be kept under immediate observation. The uterus often acts suddenly in these cases, labor may be precipitate, followed by relaxation and hemorrhage. Abnormal presentations are not infrequent, as illustrated in the case of transverse presentation described. No effort should be made to hasten labor in the interests of the child, because the fetus is so often deformed and non-viable that the mother should be exposed to no risk on its account. The placenta may separate suddenly at the latter part of labor, or may require manual removal. After the child is expelled, the uterus must be prevented from relaxing by manual compression, massage, the complete removal of the placenta and membranes, irrigation with hot antiseptic fluid, tamponing with gauze and the hypodermic use of strychnine, ergot and other stimulants, if necessary.

When a positive diagnosis cannot be made, abdominal section is justifiable to complete a diagnosis and to deal with any condition requiring removal. The uterus should not be evacuated. In a case reported by Skirving (Edinburgh Hospital Reports, vi, 387, 1900) the abdomen was opened on a mistaken diagnosis of ovarian cyst and the condition found to be polyhydramnios. The abdomen was closed, the amniotic liquid slowly disappeared and the patient went to full term and was normally delivered of a healthy, well-formed child. Such a case indicates the possibility of absorption of the excessive quantity of liquid.

Although polyhydramnios itself is nonmalignant, it has a considerable mortality-rate which is not definitely stated. Excessive distention of the uterus predisposes to relaxation and hemorrhage. Even if the fetus be not malformed, it may assume an unnatural position, and presentation upon the escape of the fluid, and be exposed to unusual danger. The mother may develop sudden shock when the

fluid is evacuated, and death from cardiac syncope may occur soon after labor. The deterioration in the patient's general health, which usually accompanies this condition, makes her more than usually susceptible to puerperal septic infection. There is every reason for thorough, prompt and skilful treatment of these cases.



CHRONIC PHAGEDÆNA DUE TO MIXED INFECTION.¹

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HISTORY OF CASE BY DR. LOUX.—J. B. McC.; aged twenty-five years; occupation, dentist; nativity, England.

Family History.—One sister died at the age of nineteen from diabetes; father is suffering from gall-stones; other than this the family history is negative.

Personal History.—Patient denied ever having chancre or chancroid. He states that at the age of sixteen years he contracted gonorrhœa, which was followed by stricture, and was treated by gradual dilatation. There was a tendency to recontract (apparently from the history of the case of resilient stricture), so much so that the patient was trained to pass his own instrument, and was instructed to do so, with the view of preventing a stricture of small calibre. He further states that there was ever present at the meatus a slight discharge of a mucopurulent character, and,

¹ From the Laboratories of the Jefferson Medical College Hospital.
Read before the Philadelphia Academy of Surgery, December 2, 1901.

as the discharge had never been examined microscopically, its character and the contained flora are not known.

Whenever the patient indulged freely in the use of alcoholic liquors, he would suffer with retention of urine, requiring catheterization.

Present History.—In January, 1901, after a night's debauch (followed by retention of urine), the patient attempted to catheterize himself, using considerable force. In the attempt he broke the catheter about one inch behind the meatus, causing a free hæmorrhage. Following this trauma to the urethra (discovered two weeks afterwards), a hard induration on the floor of the urethra appeared one inch behind the meatus; the nodule rapidly increased in size. It developed into a periurethral abscess, rupturing externally. He now consulted a surgeon, who incised the abscess freely, followed by irrigation and the usual antiseptic precautions. He further states that under this careful treatment he noticed a rapid destruction of the surrounding parts and a communication into the urethra. He was then advised to remain in the hospital, but this he refused to do.

I saw the case in consultation for the first time on February 20, 1901. The tissue on the under surface of the penis (from the frænum back one and a half inches) was destroyed apparently through a phagedænic process, involving the skin, subcutaneous tissue, and floor of urethra, including the corpus spongiosum; the skin showed the greatest resistance to the necrotic process, since the destruction extended well underneath the overlying skin, which was irregular along the edges.

The base of the diseased area was markedly indurated, not limited, but was gradually lost in the surrounding tissues, resembling the œdematous infiltration of chancroid.

On examining the urethra I found two strictures,—the first was a filiform stricture about three and a half inches from the meatus, and the second was at the bulbomembranous junction.

On March 6 I operated upon the strictures, doing an internal urethrotomy on the anterior stricture and a modified rapid dilatation on the posterior one, with continuous drainage of the

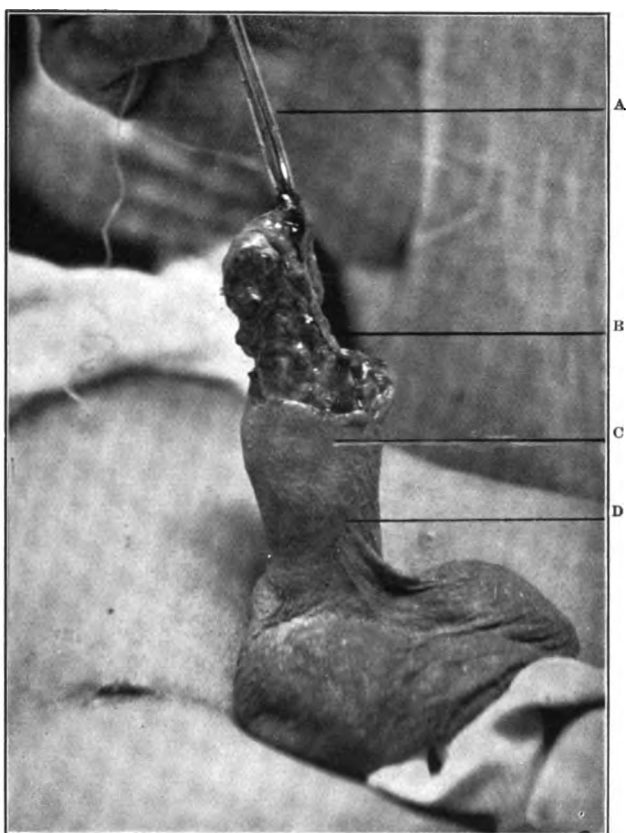


FIG. 1.—Phagedæna of the Penis. Photograph before operation. (Case reported by Dr. Loux and Dr. Coplin.) A, Hæmostat by which organ is extended. B, Fibrous septum marking superior margin of corpus spongiosum. Just below the leader from B is seen the necrosing end of the spongy body. C, The undermining extended down to about this line; at points, *e.g.*, around the urethra, the subcutaneous necrosis extended somewhat deeper. From C to D is the zone of induration. The amputation line was about the point marked by the leader from D.

bladder with a soft catheter. At the same time I curetted the necrotic area, cutting away the diseased overlying edges of skin, followed by a free application of carbolic acid to the diseased surface. Unfortunately, this did not control the phagedæna. I then decided to drain the bladder through the perineum, using a Watson tube, and attempted a plastic operation on the penis, which was done a few days after the perineal drainage was established. The plastic operation was done with great precaution, first cauterizing the surface of the ulcer, which was then removed, including the adjacent induration; a second set of instruments was used for the plastic work, which consisted in making a new urethra and covering the same and adjacent denuded area with skin flaps taken from the side of the penis. The operation was followed by primary union. The perineal tube was removed, the sinus closed, and the patient was discharged from the hospital April 2 as cured.

On April 25 the patient returned to my office with a recurrence in the right skin flap at the junction of the glans penis. The patient was placed in the hospital, and the ulcer excised by an elliptical incision, including a portion of the corona of the glans penis; the edges were brought together with a few stitches, followed by primary union. At the same time it was noticed that the corresponding left skin flap was becoming indurated, with a tendency to break down along the edges. So rapid was the destruction of the skin and deeper structures that any further operative procedure was abandoned.

An attempt was now made to control the phagedæna with the Paquelin cautery, but without any result. We then tried an application of formalin, 20 per cent. solution, which seemed to check for a short period the rapid progress of the disease. New areas then became involved; there was already much of the penis destroyed, as shown by the plate (Fig. 1), and we decided to amputate the penis at the penoscrotal junction. After his return to the hospital, it was noticed that one superficial inguinal gland on the right side was enlarged about the size of a hazel-nut; this gland showed a tendency to break down.

On September 6 the amputation of the penis was performed, and at the same time the broken-down gland of the right groin was removed; both wounds recovered primarily. There has been no recurrence of the disease to the stump of penis, but a marked recurrence in the right groin, destroying skin and superficial tissue about three and a half inches long and two inches wide. On November 6 the ulcerated area was thoroughly curetted, the diseased areas of the skin cut away, and the entire surface of the ulcer wiped out with pure nitric acid. The wound granulated, and the patient was discharged from the hospital on November 30 as cured.

PATHOLOGIC REPORT BY DR. COPLIN.—The first material for examination in this case consisted of "A," Inoculations on various media; "B," Material for spreads; "C," Fragment of tissue; all from penis.

The following is a summary of the result of the examination made by Dr. R. C. Rosenberger:

"A." Inoculations were made from the material upon glucose agar, bouillon, and liquid blood serum. Incubated for forty-eight hours, a growth was demonstrable in the glucose and urine agar. After incubation for this period, cultures were made and placed in an anaërobic condition. These cultures may be dismissed at this point, as they yielded no information not obtained by the aërobic method.

Upon urine agar there developed small, pinhead-sized colonies, yellowish in color, granular in appearance, and more or less discrete.

Spreads made from these growths and stained by the ordinary methods contain cocci .9 micron in diameter, occurring in pairs, grouped and ungrouped. Some of the pairs consist of cocci with flattened sides in apposition. They retain the dye when treated by Gram's method.

In glucose agar the growth follows the stab, and is also seen upon the surface; it is of a golden yellow color.

Spreads made and stained by ordinary methods show the same organisms described above as found in urine agar, and possessing the same morphologic and tinctorial properties.

The tubes of bouillon and serum showed a growth in seventy-two hours. Each medium was clouded, and a delicate, easily broken-up pellicle formed upon the surface.

Spreads were made and stained by ordinary methods. Upon microscopic examination two organisms were seen,—a bacillus and a coccus. The bacillus was slender, 1 micron to 3 microns in length, and .4 micron in thickness, and occurred in groups, short filaments, and ungrouped. It decolorized when treated by Gram's method.

The coccus measured .9 micron in diameter, occurring in small groups and presenting the morphologic and tinctorial characters of the staphylococci of suppuration. Plates were made, and after isolation of the organisms the bacillus was inoculated into milk, gelatin, and upon potato and other test media. Upon these different media the bacillus yielded the reactions common to organisms of the colon group,—generating a small quantity of gas, turning blue litmus red, growing with a brownish color upon potato, etc. The coccus is evidently the *Micrococcus pyogenes aureus*.

Inoculations from fresh material were also made subcutaneously into the ears of a rabbit. In seventy-two hours there was noticed swelling and redness around the site of inoculation, followed by pus formation.

Inoculations made upon plain and glycerin agar from the pus showed in forty-eight hours a pure culture of the *Micrococcus pyogenes aureus*.

Spreads made from the pus and stained by ordinary methods for bacteria contain a few polynuclear leucocytes, granular detritus, and shreds of fibrin. A few micrococci are seen, .9 micron in diameter, occurring principally ungrouped and retaining the stain when treated by Gram's method. No bacilli were demonstrable.

In six days the inflammation in the inoculated ear subsided, and since that time the animal has remained apparently healthy.

"B." Spreads made and stained by ordinary methods show numerous polymorphonuclear leucocytes and a few lymphocytes.

Numerous cocci are seen, some of which are .9 micron in diameter, occurring in small groups, but mostly ungrouped. A few are found within the cells; they retain the dye when treated by Gram's method. An occasional bacillus is seen which measures 3 microns to 4 microns in length, with rounded ends and occurring extracellular. The cocci resemble the micrococci of suppuration. The bacillus was not obtained in culture, but from its morphology resembles the *Bacillus subtilis*, probably a contaminating organism, and having no bearing upon the suppurative process.

"C." The specimen consists of a small, irregular wedge-shaped mass of tissue, .7 centimetre in its greatest, .5 centimetre in its shortest diameter, and .3 centimetre in thickness. It is of a pinkish color and the surfaces are irregular and rough.

Specimen was fixed in a saturated alcoholic solution of bichloride of mercury, and embedded in paraffin; sections were cut and stained by the usual laboratory methods.

Histologic Examinations.—One surface of the section is nearly covered by stratified squamous epithelial cells. In the middle portion of the surface the epithelial cells have entirely disappeared, or rather been converted into a mass of necrotic and richly granular *débris*. Beneath the necrotic surface a moderate degree of tissue reaction is present. The cells found here are for the most part polynuclear leucocytes, although lymphoid and spindle-shaped cells are also present in abundance. A few mast-cells are also noticeable in the sections stained with toluidin blue. Beneath the surface the mass is made up mostly of a delicate, connective-tissue reticulum. Throughout this latter tissue abundant new and newly-forming capillaries are present; some of these contain a few erythrocytes, others a few leucocytes, and still others are comparatively empty. At points a large number of polymorphonuclear leucocytes and wavy spindle-shaped cells are seen, together with a few mast-cells.

The lower surface of the mass shows a few areas of necrotic tissue, throughout which are scattered a few polymorphonuclear leucocytes.

A number of sections were stained with Löffler's methylene blue and by Gram's method.

In the preparation stained with Löffler's methylene blue a large number of bacilli and cocci are seen. Most of the bacilli are thin, 1.5 microns in length, and occur in groups and in short filaments. Where a few are seen in a field a tendency to polar staining can be recognized. This latter feature is not seen in all the bacilli. The bacilli are situated generally between the cells, though some can be seen within the cells. They do not stain by Gram's method. A second organism is a large bacillus, 3 microns to 4 microns in length, with rounded ends, occurring mostly individually.

The cocci mentioned are .9 micron in diameter, and occur principally in pairs, with their flat sides in apposition. They retain the dye when treated by Gram's method and are intra- and extra-cellular. A few other cocci are seen that are slightly smaller than those just mentioned, but possess the same peculiarities as to situation and staining reaction.

All the bacteria mentioned above are scattered through the specimen. They are most abundant deep in the tissue, although some (bacilli and cocci) are found in the most superficial layers of the necrotic epithelial cells. The small bacillus referred to resembles very closely the bacillus of Ducrey, both morphologically and tinctorially. Every peculiarity of the bacillus, however, is not present, but the size, situation, and staining properties suggest this probability very strongly. The cocci are undoubtedly the ordinary micrococci of suppuration.

Diagnosis.—"A." Inoculations upon glucose and urine agar. Pure culture of the *Staphylococcus pyogenes aureus*. Inoculations in bouillon and liquid serum, a bacillus probably of the colon group and the *Staphylococcus pyogenes aureus*.

"B." The spreads contain cocci possessing the usual morphology and tinctorial reactions of the micrococci of suppuration.

"C." The tissue shows a widely destructive inflammation, the necrosis being of the liquefaction type. Bacteria are present in abundance; one of the organisms present cannot be differentiated from the bacillus described by Ducrey; it is not our inten-

tion, however, to insist upon the identity of the germ found with the microbe described by that observer. The histology of the tissue excludes malignant disease. At the time of this examination tuberculosis was not suspected, even after most careful search for the bacillus as well as close study of the histology of tissue submitted.

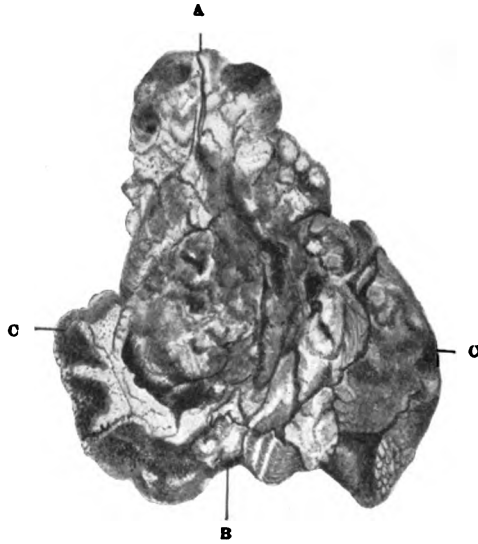


FIG. 2.—Penis after amputation; inferior surface. Natural size. (Case reported by Dr. Loux and Dr. Coplin.) A, Fissured ulcer marking area of urethra beneath the glans. B, Urethra at point of amputation; laid open. C C, Undermined skin incised on inferior surface and turned back (dorsalwards) in order to indicate the extent of the undermining. Just below the leaders from C C the intense induration is indicated.

Result of the examination of the amputated penis. The specimen delivered to the laboratory consists of an irregular cylindric mass of tissue measuring 8 centimetres in length. (Fig. 2.) One end of the cylinder is surrounded by skin, which at the extreme end is normal in appearance. This end measures 3.5 centimetres in diameter, and evidently corresponds to the line of amputation. The corpora cavernosa are somewhat retracted

below the surface and appear slightly denser than normal, the right being somewhat more resistant than the left. The spongy body—corpus spongiosum—is inconspicuous, but the urethra can readily be identified in its centre. The subcutaneous tissue and the tunica albuginea present nothing noteworthy. Upon laying the urethra open, it is found that its length does not exceed 0.5 centimetre. Its mucous membrane at the line of incision is apparently normal, but at the external opening is ragged and ulcerated and undermined to within 0.3 centimetre of the line of incision. The width of the band of attached skin varies; at its widest point it is 4.5 centimetres, and at its narrowest point a little less than 2 centimetres. As already stated, the skin is normal along the line of incision. The free margin of the skin is ulcerated, ragged, undermined, and presents areas of superficial necrosis which extend from 5 to 20 millimetres from the free margin of the ulcer upward and backward upon the otherwise normal skin. The free margin of this ulcerated portion is slightly indurated, the amount of induration varying in different areas. At all points the margin is undermined, and in the neighborhood of the urethra the undermining at one point extends 2.5 centimetres. The urethra for a distance of about 4.5 centimetres has been entirely destroyed, and with it practically all of the spongy body. The glans has been for the most part destroyed. The remaining portion of the glans measures 3 centimetres by 2 centimetres. The superior surface of the glans (all the remaining portion) is covered by a wrinkled mucosa, the margin of which forms the ragged, indurated, and necrotic edge of the ulcer. There is but little undermining of the mucosa. The surface of the ulceration is beset with minute granules and covered by a grayish pellicle which can be removed with very little manipulation. The ulcerated portion is somewhat indurated, the degree of induration varies in different parts, but is usually more marked near the margins of the ulcer.

Small masses were cut from different areas, fixed, dehydrated, and embedded in paraffin.

Sections cut from the region of the glans show the specimen

to be covered by stratified squamous epithelial cells. Beneath the epithelium is a quantity of loose connective tissue and a few bundles of non-striated muscle.

Sections taken from the dorsum of the penis (Fig. 3) show it to be covered by stratified squamous epithelium upon one surface. Beneath this epithelial layer is a large quantity of rather

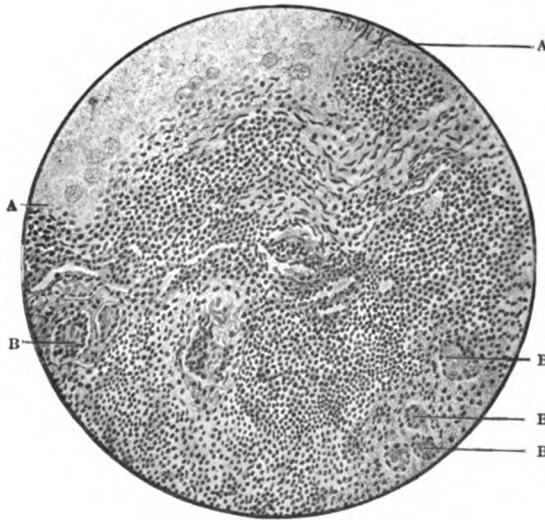


FIG. 3.—Section of floor of ulcer, case of chronic phagedæna. (Reported by Dr. Loux and Dr. Coplin.) A, A, The area between these two points is superficial and composed of the tissue undergoing liquefaction necrosis. Aside from the contained granules, a few granular and necrotic cells showing fragmentation and karyolysis are also present. B, B, B, B, Giant cells; other giant cells are also seen at several points in the field. Lymphoid cells are abundant throughout the field, and just above the centre and to the right are a number of fibroblasts. No area of caseation is present in this field.

dense connective tissue and non-striated muscle. Here and there can be seen accumulations of small round cells, polymorphonuclear leucocytes, a few epithelioid cells, and giant cells,—distinctly suggestive of tubercles.

They are for the most part discrete, but in one or two areas

a beginning coalescence of two tubercle-like agminations can be detected. Beginning caseation is also noticeable in other areas.

Sections taken from the region of the urethra show the mass to consist almost wholly of granulation tissue. The lining epithelium of the urethra is in some parts destroyed and encroached upon by the granulation tissue. No well marked tubercles are seen in these sections, but a few giant cells are scattered throughout. The sections were also stained for bacteria, and especially for the tubercle bacillus.

Upon examination of sections stained with Löffler's methy-

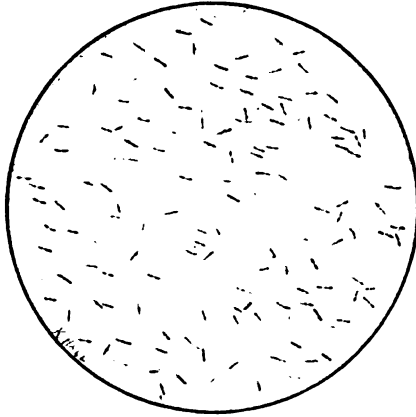


FIG. 4.—Bacillus of soft chancre (Ducrey). The irregular staining of the organism and variations in morphology are well shown. From section stained with methylene blue. Zeiss 2 mm. homo. im., projection eyepiece No. 2.

lene blue, in the blood-vessels, intracellular and scattered irregularly through the tissue, numberless bacilli were demonstrable. They average 1.5 microns in length, possess rounded ends, and exhibit polar staining. They do not retain the dye when treated by Gram's method. (These bacilli are similar to the organisms met with in sections from the same case made some time before, and which were then thought to be the bacilli of Ducrey.) A few cocci were also seen. No tubercle bacilli nor any other acid resisting bacilli were demonstrable.

The tissue removed from the groin was not examined; it was ordered sent to the laboratory, but was not delivered in a condition permitting examination.

Diagnosis and Remarks.—The process is clearly not a simple one. The profound tissue alterations are evidently the result of a violent infection, mixed in character, and rapidly extending; a careful histologic study fails to show satisfactory evidence that the tissues are making any efficient effort to limit the spread of the bacteria. Not only do the bacterial findings clearly show the existence of a mixed infection, but the histology discloses the presence of two forms of necrosis occurring separately and only together in the sense that one may be consecutive to the other, a view not supported by a study of the sections. The liquefaction necrosis is evident superficially, restricted to the skin and outer layer of granulation tissue, while the caseation is present at or near the areas of giant cell agmination and not evident elsewhere. Our inability to demonstrate the tubercle bacillus in its usual form, or in some of its so-called involution types, does not exclude tuberculosis, but leaves the one essential link missing; personally, I am strongly inclined to urge the presence of tuberculosis as a part of the infection. The pyogenic infection is of course demonstrated, but space precludes its further discussion. The suppurative process induced experimentally seemed to differ in no essential from staphylococcic infections frequently seen.

Probably the most important point to be settled, if settled it can be, is whether the fundamental lesion in this case was chancroidal; should we accept the bacillus of Ducrey as the cause of soft chancre, then the bacteriologic findings are to be weighed against the clinical aspects of the case. If the clinicians decide that the lesion is not chancroid, then the bacteriologic finding is of still greater import, as I think we have demonstrated the presence of an organism that at least cannot

be differentiated from the bacillus in question if it be another germ.

The bacillus of Ducrey¹ (Fig. 4) is given by Cornil and Ranvier² as the cause of chancroid. After the appearance of the papers by Krefling³ and Unna,⁴ I sectioned a number of soft chancres and studied the pus from others. I was greatly impressed with the constancy of the organism, although occasionally I examined lesions, clinically thought to be typical instances of chancroid, in which the organism could not be found. Since that time, Peterson,⁵ Nicolle,⁶ Istamanoff and Akspiantz,⁷ Leuglet,⁸ F. Bezançon, V. Griffon, and Le Sovrd,⁹ and others have done much to establish the specificity of the organism described by Ducrey. Nicolle maintains the value of finding the organism as a test differentiation from the initial lesion of syphilis.

If the writers quoted, and others that could be mentioned, are correct in their view, then the case is one of chancroid running an unusually lengthy course and with an unusual destruction of tissue. Although, as already stated, we have failed to demonstrate the tubercle bacillus, I cannot ignore the histologic picture quite faithfully portrayed in some of the sections. Admitting the doubtful points, this lesion would be regarded as a manifestation of (1) staphylococcic infection, (2) infection by the colon bacillus, (3) infection by the streptobacillus of Ducrey, and (4) tuberculosis, the morbid processes not necessarily occurring in the order given.

[NOTE.—Since the foregoing report was submitted there have been no recurrences at points of previous operations. About the middle of February, 1902, the left epididymis became tender and slightly enlarged, and rapidly increased in size. On March 4, Dr. Loux removed the left testicle with the cord as far as the left external ring; although the examination is not as yet completed, it is sufficiently advanced fully to establish the diagnosis, and proves the testicular enlargement to be due to an acute,

rather disseminated tuberculosis involving both the globus major and globus minor.

In the light of the added information, the conclusion previously reached, that the condition was primarily either chancroidal or septic, the probabilities favoring the former, and that upon the initial infection was engrafted tuberculosis, seems to be thoroughly established.]

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THE BACTERIOLOGIC EXAMINATION OF CLINICAL THERMOMETERS.

BY

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I have been impressed with the fact that while surgeons, obstetricians, and many specialists recognize the necessity of guarding against infection by the sterilization of instruments used in operations as well as instruments of precision, the general practitioner not infrequently entirely neglects such precautions, especially in the use of tongue-depressors and thermometers. Upon inquiry many of the general practitioners have been found to make an attempt to limit infection by thermometers, resorting to some antiseptic or germicide kept in the thermometer case. While admitting the possible efficacy of such a method, its routine use in the careless manner commonly adopted is probably more dangerous than no attempt at disinfection, because an inefficient and unreliable method offers a sense of security not at all justified.

One physician whose thermometer I examined used a 1% solution of formalin, with which he saturated a small pledget of cotton kept in the thermometer case. Another practitioner applied carbolic acid in a similar manner. Upon the examination, however, of these containers and the enclosed cotton neither formalin nor carbolic acid could be detected by odor and the bacteriologic findings demonstrated their inefficiency. It is unnecessary to say that the customary habit of simply rinsing a thermometer in water and wiping the instrument on a towel or handkerchief affords no protection.

A series of experiments have been made for the purpose of determining, so far as possible in a small number

of cases the probabilities of infection by means of a thermometer.

The method pursued was (1) to obtain the diagnosis of the case in which the thermometer was last used; (2) the time that had elapsed since the instrument was used; (3) how the thermometer was cleansed after using.

Technic of Examination.—Having obtained the information indicated in the foregoing, the next step was to infect melted agar from which plates were made. The method of making plates was as follows:

A petri dish was sterilized and half a tube of melted agar poured upon the bottom dish. With a sterilized glass brush (made sterile by passing directly through the Bunsen flame) the degree marks were thoroughly brushed upon the agar spread in the dish. The lid was lifted carefully and quickly, and as quickly replaced. In the remaining half of the melted agar in the tube, the thermometer was rotated for a few minutes, then withdrawn, the tube agitated, and its contents poured into the dish containing the first part of the agar, and the lid replaced. The plate was then allowed to set.

Inoculations were also made in bouillon by rotating the thermometer in the medium which was then set aside for 24 or 36 hours, and when cloudiness appeared, plates of agar were made. The results obtained by this method were used only for the purpose of establishing the character of the organisms present, being controls to the agar plates made as already described.

The next procedure was to observe how many colonies developed in the agar plates and what bacteria were present. The following is a detailed list of some of the examinations made and the results:

A thermometer used in a case of bronchopneumonia in a child was washed in cold water, dried with a handkerchief, and examined 2 hours later. In 48 hours, 46 colonies had developed; 17 of these were *Staphylococcus pyogenes albus*; 2 colonies were *Staphylococcus pyogenes aureus*; the remaining were *sarcinae* and yeasts.

A thermometer used in a case of diphtheria was washed with cold water, dried with a handkerchief, and examined 48 hours later. The plate yielded 12 colonies; 7 of these were *Staphylococci* (*pyogenes albus* and *aureus*), and the remainder were *sarcinae*.

A thermometer used in a case of tuberculosis (pulmonary) was cleansed as were the foregoing, and examined 48 hours later. The plate developed 1 colony of the *Staphylococcus pyogenes albus* and 2 colonies composed

of sarcinae. The physician from whom the thermometer was obtained used carbolic acid in the thermometer case.

From a thermometer that had not been used for 42 days, and where the physician had forgotten the diagnosis of the case in which the instrument was last applied, there developed 6 colonies. Of these, 2 were *Staphylococci*, 1 was evidently a member of the colon group, and 3 were sarcinae.

A thermometer used in a case of rheumatism and immediately washed in a 5% solution of carbolic acid was examined 72 hours later, and yielded at the end of 48 hours' cultivation, 12 colonies; 3 were *Staphylococcus pyogenes albus*; 5 sarcinae; 1 *Bacillus subtilis*, and 3 of a chromogenic (pink) diplococcus.

A thermometer used in a case of pulmonary tuberculosis was washed in cold water, dried with a handkerchief, and examined 56 days later. In 48 hours 15 colonies developed; 4 of these were *Staphylococci*; 6 were sarcinae; 3 *Bacillus subtilis*; 2 chromogenic (pink) diplococcus.

TABLE I.

Cases.	Length of time after using.	No. of Colonies.	Bacteria found.
Bronchopneumonia .	56 days	46	<i>Staphylococci</i> , 19 colonies <i>Sarcinae</i> , 27 "
Diphtheria	48 hrs.	12	<i>Staphylococci</i> , 7 " <i>Sarcinae</i> , 5 "
Tuberculosis	48 hrs.	3	<i>Staphylococci</i> , 1 " <i>Sarcinae</i> , 2 "
Rheumatism	72 hrs.	12	<i>Staphylococci</i> , 3 " <i>Sarcinae</i> , 5 " Diplococcus (pink), 3 col. <i>B. subtilis</i> , 1 colony
Tuberculosis	46 days	15	<i>Staphylococci</i> , 4 " <i>Sarcinae</i> , 6 " <i>B. subtilis</i> , 3 " Diplococcus (pink), 2 col.
Puerperium	24 hrs.	16	<i>Staphylococci</i> , 2 colonies <i>Sarcinae</i> , 6 " Diplococcus (pink), 4 col. <i>B. subtilis</i> , 4 colonies
Diphtheria	48 hrs.	24	<i>Staphylococci</i> , 6 " Pseudodiphtheria bacillus, 1 colony <i>Sarcinae</i> , 17 colonies
Not given	42 days	6	<i>Staphylococci</i> , 2 " <i>Sarcinae</i> , 3 " <i>B. coli communis</i> , 1 col.

A thermometer used during the puerperium was washed with cold water, dried with a handkerchief, and examined 24 hours after the last time it was used. Plates contained 2 colonies of the *Staphylococcus*; 4 *Bacillus subtilis*; 6 of the *sarcinae*, and 4 of the chromogenic (pink) diplococcus.

TABLE II.

Cases.	Length of time after using.	No. of Colonies.	Bacteria found.
Chronic indigestion .	24 hrs.	4	<i>Staphylococci</i> , 3 colonies
Chronic indigestion .	3 hrs.	14	<i>Sarcinae lutea</i> , 1 "
			<i>Staphylococci</i> , 10 "
			<i>Yeast fungi</i> , 3 "
			<i>B. subtilis</i> , 1 "
Chronic indigestion .	12 hrs.	12	<i>Staphylococci</i> , 11 "
			<i>Yeast fungi</i> , 1 "
Chronic interstitial nephritis	24 hrs.	6	<i>Staphylococci</i> , 2 "
			<i>B. subtilis</i> , 4 "
Gout	48 hrs.	4	<i>B. subtilis</i> , 4 "
Measles	24 hrs.	20	<i>Staphylococci</i> , 11 "
			<i>B. subtilis</i> , 5 "
			Unidentified bacilli, 4 "
Measles	48 hrs.	6	<i>Staphylococci</i> , 5 "
			<i>B. subtilis</i> , 1 "
Measles	8 hrs.	26	<i>Staphylococci</i> , 22 "
			<i>Sarcinae lutea</i> , 4 "
Scarlet fever	12 hrs.	24	<i>Staphylococci</i> , 18 "
			<i>Sarcinae lutea</i> , 4 "
			<i>B. subtilis</i> , 2 "
Scarlet fever	24 hrs.	18	<i>Staphylococci</i> , 12 "
			<i>Sarcinae lutea</i> , 4 "
			<i>B. subtilis</i> , 2 "
Tuberculosis	36 hrs.	6	<i>Staphylococci</i> , 4 "
			<i>Sarcinae lutea</i> , 2 "
Tuberculosis	24 hrs.	16	<i>Staphylococci</i> , 6 "
			<i>B. subtilis</i> , 4 "
			<i>Sarcinae lutea</i> , 6 "
Tuberculosis	72 hrs.	2	<i>Staphylococci</i> , 2 "
Tuberculosis	48 hrs.	6	<i>Staphylococci</i> , 4 "
			<i>Sarcinae lutea</i> , 2 "
Tuberculosis	8 hrs.	22	<i>Staphylococci</i> , 12 "
			<i>B. subtilis</i> , 8 "
			<i>Sarcinae</i> , 2 "
Diphtheria	24 hrs.	4	<i>Streptococci</i> , 1 "
			<i>B. subtilis</i> , 3 "
Bronchitis	72 hrs.	6	<i>Staphylococci</i> , 4 "
			<i>B. subtilis</i> , 2 "
Bronchitis	24 hrs.	12	<i>Staphylococci</i> , 8 "
			<i>Yeast fungi</i> , 4 "
Bronchitis	12 hrs.	28	<i>Staphylococci</i> , 10 "
			<i>Sarcinae lutea</i> , 10 "
			<i>B. subtilis</i> , 6 "

A thermometer was obtained from a physician who had used the instrument in a case of diphtheria, washed it in water, and later took his own temperature, again cleansing the instrument as in the first instance. I examined the thermometer 24 hours later. The cultures yielded 24 colonies; 6 of *Staphylococcus pyogenes albus*; 1 of a bacillus which I was inclined to regard as the pseudodiphtheria bacillus, and 17 colonies of *sarcinae*.

Without going further into the details of the examination in various cases, the following tables are submitted:

Table I is the result of the examination of thermometers used in the mouth, and Table II of thermometers used in the axilla.

TABLE III.

Cases.	Length of time after using.	Result.
Rheumatism	1 hour	Sterile
Chronic interstitial nephritis	2 hours	"
Croupous pneumonia	1 hour	"
Enteric fever	3 hours	"
Bronchitis	2 hours	"
Chronic indigestion	1 hour	"
Influenza	2 hours	"
Influenza	2 hours	"
Acute parenchymatous nephritis	1 hour	"

An examination of the results yielded by this investigation would satisfy the most skeptical that thermometers can readily transmit the bacterial flora found in the oral cavity. The writer is aware that for the satisfactory completion of this inquiry it would have been necessary to examine the secretions in the mouths of the patients upon whom the thermometers were used, and to have satisfied himself as to the character of the bacteria that they contained. There is another source of danger into which the inquiry did not extend, infectivity of thermometer cases, but as the case would only be a carrier, the essential danger, if any exist, must be in the thermometer. In order to determine how readily thermometers could be disinfected the writer made 9 experiments, using the following technic:—

Immediately after removal from the mouth the thermometer was washed in water, immersed in corrosive

sublimate for 2 minutes, removed from the antiseptic, dried in the air, and replaced in the case. Later the instruments were examined, using the same technic as detailed above.

The results of these experiments are given in Table III.

CONCLUSIONS.

1. It is possible for the thermometer to be laden with the usual flora of the oral cavity.
2. Such bacteria may retain their capability of growth for an indefinite time, at least 2 months, as shown by the above experiments.
3. Many pathogenic bacteria possess similar capabilities, and it is not unreasonable to assume, although the above experiments are not conclusive upon this point, that transmission of bacterial disease by the thermometer is possible.
4. Thermometers are easily disinfected.
5. Where possible each patient should be possessed of a thermometer, as much his own property, and as sacred to his own use as his toothbrush.
6. Where for reasons of economy or otherwise it is impossible to carry out the recommendations expressed in conclusion 5, the thermometer should be disinfected before and after using.
7. The custom now prevalent in the hospitals of keeping thermometers in disinfecting solutions is to be commended.

**CONGENITAL DISLOCATION OF THE HIP: REPORT
OF A BLOODLESS REPOSITION, FOLLOWED BY
DEATH, WITH AN ANALYSIS OF TWENTY-
THREE CASES IN PROCESS OF TREATMENT.**

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PATHOLOGIC REPORT BY

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The clinics held by Professor Adolf Lorenz on December 11 and 12, 1902, at the Jefferson Medical College Hospital and the widespread accounts of his methods and skill naturally attracted many people to his bloodless methods of reduction of congenital dislocation of the hip. Many patients were brought for treatment by the noncutting method that were beyond the age limit set by Lorenz and often positively refused to have even subcutaneous tenotomy performed. This will explain the fact that patients beyond the age of 7 were operated upon by the bloodless method that were considered too old for that method, and yet at least three cases were found to present conditions that rendered the reduction much easier than in some of the younger children.

All of the patients that have been operated upon at the Jefferson Hospital during and since the Lorenz clinics are in process of treatment, as six months from the time of operation have not yet elapsed. It is proper to speak of them at this time only as to the reduction and later when their plaster casts are removed the results can be determined.

Case No.	Name.	Sex.	Age.	Date.		Operator.
1 and 2.	R. C.	Girl.	21 months.	Dec. 11.	Double.	Lorenz, assisted by Müller, Ashley, Wilson, Rugh, Dolson, and Taggart.
3.	R. E. C.	Boy.	20 "	"	Left.	
4.	A. P.	Girl.	9 years.	"	"	
5 and 6.	M. I.	"	4 "	"	Double	
7 and 8.	M. G.	"	4 "	Dec. 12	"	Wilson, assisted by Rugh, Dolson, and Taggart.
9.	G. R.	"	7 "	Mar. 8.	Left.	
10 and 11.	H. L.	"	2 "	Feb. 6.	Double.	
12.	K. C.	"	7 "	Jan. 7.	Left.	
13.	A. H.	Boy.	4 "	Mar. 2.	Right.	Wilson, assisted by Rugh, Dolson, and Taggart.
14 and 15.	E. K.	"	10 "	Feb. 11.	Double.	
16.	M. H.	Girl.	8 "	Mar. 21.	Right.	
17.	R. M.	"	7 "	Mar. 8.	Left.	
18 and 19.	B. D.	"	7 "	Mar. 18.	Double.	Rugh.
20.	E. R.	Boy.	9½ "	Apr. 15.	Left.	
21.	R. M.	Girl.	3 "	Apr. 20	"	
22.	K. McF	"	3 "	Feb. 1.	"	
23.	J. S.	Boy.	18 months	Mar. 8.	"	

12 girls { 5 double
 { 7 single { 5 left.
 { 2 right.
 5 boys { 1 double
 { 4 single { 8 left.
 { 1 right.
 Total { 6 double
 { 11 single { 8 left.
 { 3 right.

6 cases 2 years and under.
 2 cases 2 to 3 years of age.
 5 cases 3 to 4 years of age.
 5 cases 6 to 7 years of age.
 3 cases 8 to 9 years of age.
 2 cases 10 years of age.

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The members of the orthopedic department who assisted Dr. Lorenz on December 11 and 12 were H. Augustus Wilson, J. Torrance Rugh, F. E. Dolson, T. D. Taggart, with G. J. Schwartz etherizer, supplemented by Dr. Frederick Müller and D. D. Ashley. The 23 hips operated upon include 8 done by Lorenz and the above-named assistants, 18 done conjointly by the staff of the orthopedic department, and 2 done outside of the hospital by Dr. Rugh. The details as practised by Lorenz have been most critically carried out. It was deemed unwise to attempt the least departure from the methods which Lorenz with his vast experience and consummate skill had demonstrated before a most critical audience of 700 medical men. That we lacked his ability was, of course, to be expected, but each of us became more and more convinced with each case that in suitable cases great force was unnecessary when skilful manipulations were employed. The very great force that is sometimes spoken of in connection with this

method is employed only in those older patients in whom use has developed strong and resistant muscles and fibrous materials in relations with the hip or when unsuccessful attempts have been made at reduction.

Professor Lorenz found the reduction to be accomplished with ease in the first four hips, notwithstanding that one of the patients was 9 years of age. The next one, aged 4, proved to be extremely difficult, and taxed Dr. Lorenz's skill and strength almost to the limit, but finally yielded and demonstrated a satisfactory reduction.

The last patient, aged 4, with double dislocation, had been placed under ether to be in readiness, but could not be operated upon because of the difficulties encountered in the former case. The child had been under ether for 35 minutes before it was decided to postpone reduction in her case. She made a satisfactory return to consciousness. The day following she was again etherized, and Dr. Lorenz reduced both hips. She went to the ward in good condition at 6 p.m.

The following notes are given by Dr. P. H. Moore, the house surgeon. The phenomena were also witnessed by Dr. Wilson :

At 9.15 p.m. the right hand was observed to begin to move in an indefinite, convulsive manner, and the patient rapidly passed into a state of stupor; the eyes became fixed, pupils dilated and did not respond to light; the tongue protruded, and froth-like saliva dribbled from the mouth. The face was markedly pallid and cold. Breathing was somewhat slower than normal and labored. Occasionally the lower jaw moved slightly, but there was no biting of the tongue. The pulse was not rapid, but decidedly weak. Later it became rapid, and could not be counted owing to arm movements. The right leg was several degrees lower in temperature than the left, and offered almost no resistance to manipulation. In three-quarters of an hour the stupor began to lessen; respiration became more nearly normal. A slight flush came to the cheeks, the tongue retracted, and the muscles of the face showed some twitching movements. The right hand underwent convulsive movements, the head was turned violently from side to side; there were mild clonic convulsions of the muscles of the back, and speech, slowly restored, became coherent. In about 1½ hours the condition was practically the same as before the attack. The child did not sleep. At 12.30 (same night) there was a much briefer attack, showing some of the above phenomena in modified form. Restless sleep until morning. There was no recurrence, and no resulting paralysis. The child was languid.

Professor Lorenz, in a personal communication, said (after reading the above record of the phenomena) that he had never had a case in which convulsions followed

the operation, and he considered shock and trauma as the cause of this case.

K. C. The radiograph was relied upon, and it showed the condition of the acetabulum and the head of the femur to be favorable. There had been a cutting operation performed two years previously, and it was stated that this was for the evacuation of an abscess. The head of the bone seemed to be easily pulled down to Nélaton's line before the reduction was attempted. It was discovered later, during the manipulations, that there was no head to the femur, and we inferred that it had been removed at the operation referred to. It was found to be impossible to obtain any information as to what was really done, although careful inquiries were instituted. The hospital where the child was operated upon was under a staff that was not in affiliation with members of the American Medical Association.

M. H. Some considerable edema of the right labium majus developed about 10 hours after reduction of the hip, which necessitated catheterization for 24 hours, but it then subsided and normal functions were reestablished.

With these few exceptions the patients all progressed favorably, and after remaining quietly in bed for from three to four days, were permitted to sit up, and were usually sent out of the hospital within a week from the time of operation. They were kept under observation by physicians in attendance upon the families and reports were made to the Jefferson Hospital from time to time.

In not one case has there been any evidence of paralysis or other nerve disturbance. Pain on attempting to use the leg operated upon has generally persisted for two to four days, and after that was only present when the hamstring tendons were stretched in those cases in which some flexion of the knee persisted. This, however, soon subsided, and freedom from pain or annoyances of any kind has been the condition in all cases excepting only the inconvenience of the plaster cast and the position in which it held the leg. It was a matter of great interest to see how quickly the children learned to adapt themselves to the posture of the affected leg, and to use it in walking where only one hip had been replaced.

We were surprised to see how little attention Lorenz paid to the very carefully prepared skiagrams that accompanied each of the 20 cases submitted to his inspection and selection for his clinics on December 11 and 12. His reliance on clinical inspection of the case, the thor-

ough manner in which he determined the existing conditions and the prospects for reduction, impressed every one with his rapidity and certainty of action and decision.

Subsequent experience has convinced us that the well recognized possibility of variously interpreting radiograms renders their use of much less real value than would naturally be supposed.

It cannot be disputed that aid can be obtained from a careful study of a radiogram in direct connection with the analysis of the clinical phenomena, but the latter are to be relied upon for definite facts as to the condition of those factors about the joint other than bone which play equally important parts in resistance to reduction. In the case of M. I., which Professor Lorenz found the most difficult of all to reduce, the radiograph showed a most favorable condition, and was therefore most misleading. The same thing has been found in several other cases, notably in E. K., age 10 years, and the radiograph indicated unfavorable conditions for the bloodless method, which was attempted only as a preliminary measure in order to prepare him for a cutting operation to be performed later in accordance with the teaching of Lorenz. Reduction, however, was accomplished by us with far greater ease and certainty than in many of the other cases.

The only fatal result is here fully recorded.

On March 10, 1903, B. D., a girl, aged 7½, was first seen by Dr. Rugh, she having been sent by the family physician, Dr. I. A. Fries. The family history showed tuberculosis on the father's side, a brother having died of pulmonary tuberculosis, but no history of any similar deformities on either side of the family.

The patient was the oldest of three children, the second one, however, died in its fourth year from meningitis. Birth of the patient was normal. She had measles at three years of age. All three of the children had very large heads when born and the disproportion remained quite marked, giving the appearance of hydrocephalus. Patient never was a robust child nor a hearty eater, but seldom complained of illness. When nearing two years of age she began to walk and the family physician began to notice that she appeared much shorter when standing than when lying. A careful examination revealed to him a double congenital misplacement of both hips upward and backward on the dorsum illi. He immediately sent her to the orthopedic department of a hospital in this city where she remained under treatment for nearly two years. The treatment consisted in extension for over a year and then the application of plaster-of-paris with the legs in the position of slight flexion and slight abduction. Radiographs taken at the time showed the heads of the femurs to be *opposite* to but not *in* the acetabula. Braces were later applied and worn for two years, but the hips remained misplaced and her gait was very much impaired. When she was examined on March 10, and later, she

presented the following appearance: A rather delicate looking child of ordinary height and somewhat under weight. The calvarium was very broad, the face somewhat narrow, accentuating the rachitic tendency, and the veins of the forehead and neck were quite prominent. The skin was almost transparent and presented a very waxy appearance. The chest was spare but of normal size; the abdomen retracted; the extremities thin and the muscles weak. There was marked lordosis of the lumbar spine and the gait was very awkward and rolling. The knees presented a pronounced condition of genu recurvatum and knocked together in walking. The ligaments of the several joints of the lower extremities were very much relaxed, allowing considerable abnormal motion. The feet were in the position of valgus and the toes were markedly everted. The hips were very freely movable and on standing the femoral heads and trochanters stood out prominently. They could be drawn down to the acetabula but not oppositiz. Muscular control was good but the muscles were weak. The adductors were very much shortened as were also the flexors, and the thighs could not be abducted in the line of right-angled flexion beyond 45°. The radiograph showed fairly well-developed femoral heads and acetabula. There being no apparent counterindication present, bloodless reposition was advised and assented to by the parents after the dangers were outlined to them. The patient entered the Jefferson Hospital on March 17, and was prepared for operation in the manner usual at that institution, viz., regulation of the diet, bowels and secretions, with rest in bed for a period of not less than 24 hours. The examination of the heart and lungs was negative and the urine examination was as follows: Urine clear, straw color, acid reaction, faint trace of albumin, 1.5% urea, amorphous urates, squamous epithelial cells and a few leukocytes. The operations were performed the following day at 11 o'clock by the writers, assisted by Drs. Dolson and Taggart, and the anesthetic was administered by Dr. G. J. Schwartz, the official anesthetizer for the orthopedic department. The right hip was first attempted, the various steps of stretching and tearing the adductors and flexors being carefully followed out, and then external rotation and circumduction with hyperextension in the abducted position was employed but reduction failed. A very significant thing occurred while tearing the adductors, but was considered at the time as not having any special significance. As soon as abduction was made in the tearing of the adductors the skin over these prominent muscles where massage was used began to tear, showing the low state of vitality present. This occurred on both sides, and wherever pressure was made by the hands, or means of reduction, a blue mark appeared.

After several more attempts in the same manner were made the yarn rope was attached to the ankle and traction made to stretch the capsule downward as well as to bring the head opposite the acetabulum. The hip was manipulated while this was being done and then reduction was again attempted but was not accomplished. While the hamstrings were being stretched something was heard to snap and it was thought to be the tendons of the semitendinosus or semimembranosus muscles, but this was evidently when the ischium was fractured, although it did not seem like a bone breaking. When traction was being made on the femur, a tearing sound was noted and was supposed to be the Y-ligament, but evidently the femoral neck was fractured instead, although it could not

be recognized at the time. After 25 minutes work by both operators the head was thought to be placed upon the acetabulum, as the leg could not be straightened at the knee, and this was given by Lorenz as the sign of replacement.

The child's condition seemed good and it was decided to attempt the reduction of the left hip at once. No greater difficulties to reduction appeared in the left leg than were encountered in the similar stages with the right, but the skin likewise gave way over the adductor tendons. The strong resistance of the hamstring tendons induced the operators to cease further efforts after 15 minutes time when it was realized that reduction by the bloodless method was impossible without unduly prolonging the manipulations that were made. It was decided to place the legs in the best possible position for repair of the torn structures and subsequently to resort to the intermediary operation of cutting down upon the joint and stretching the capsule and removing such other obstacles as might be found. When the legs were in position for the plaster casts it was found that the left leg like the right gave the test condition of resistance to extension of the leg and led the operators to believe that the head on this side also rested on the acetabulum. The error in this respect was demonstrated at the postmortem. Both legs were then placed in the position of hyperabduction and hyperextension ("frog position") and plaster-of-paris applied by Drs. Dolson and Taggart.

The following notes are given by Dr. C. A. Dexter, the house surgeon :

The child was brought up from clinic at 12.30 o'clock. The pulse was rather weak and rapid, and atropin sulfate, .3 mg. ($\frac{1}{100}$ grain) and strychnin sulfate 2 mg. ($\frac{1}{50}$ grain) were given hypodermically and external heat applied, and the child reacted very well. On coming from under the influence of ether about two hours later appeared to be in fair general condition. Later in the afternoon complained of some thirst, but not so much as the average ether patient. Was a little restless, but not so much as the usual case of a reduction by the same method. Was not nauseated and did not vomit during the afternoon. About 9 o'clock p.m. vomited about two ounces of a dark brownish fluid and once or twice during the night after this. Had stimulation during the night. After 10 p.m. the child became delirious, the delirium being of a mild talkative character and continuing throughout the night. At 8 o'clock a.m. the temperature was down to 97° and external heat was applied. Pulse was somewhat rapid and weak, and coffee and whisky by enema, atropin and strychnia hypodermically were given. The child apparently had begun to react, the pulse getting stronger. Was now perfectly conscious and said that she was not in any pain.

At 9 a.m. Professor Wilson was telephoned for and arrived ten minutes later. Instruments were in readiness for saline infusion, but the child's condition became so rapidly worse that an opportunity to use them was not given.

At 9.35 a.m. her condition seemed somewhat improved.

At 9.40 a.m. there was a marked change; breathing suddenly became gasping and superficial; pulse absent at the wrist; stimulation was again used hypodermically, but the breathing quickly became worse, the heart-beats weaker, and with a few convulsive gasps the child died at 9.45 a.m.

TEMPERATURE CHART.

Date.	Hour.	Resp.	Pulse.	Temperature.
March 17.	4 p.m.	20	90	98.4°
" 18.	8 a.m.	20	80	97.0°
" 18.	1 p.m.	82	100	98.0° after operation.
" 18.	3 p.m.	82	112	101.0°
" 18.	6 p.m.	86	104	101.4°
" 19.	5 a.m.	88	132	98.4°
" 19.	9 a.m.	40	156	99.4°
" 19.	9.45 a.m., died.			

In the light afforded by the very careful postmortem examination by Dr. Coplin in the presence of the staff of the orthopedic department, it may be noted that this was a case in which replacement could not have been secured without removing the ligamentum teres, and that there was no way of predetermining the existence of the obstacles to the bloodless reposition.

The main factor was the length and size of the ligamentum teres, which more than filled the acetabulum on each side, and therefore the sign which indicates reduction—that is, the slipping out of the head from the acetabulum as the leg is brought into an extended position—was absent. While this one factor, *i. e.*, the ligamentum teres, was sufficient to have prevented reduction, the very thick capsule was elongated and had a tendency to fold in between the head and the acetabulum again, preventing the clear sound that occurred in other cases when the head, it is believed, entered the acetabulum. On both sides the articulating surface of the head was found placed above the posterior rim of the acetabulum, in which position it was placed at the time of operation, and was, therefore, decidedly anterior to the position which it had formerly occupied on the dorsum of the ilium. Just when or how the three fractures occurred it is impossible to determine, for while something was felt by the operators which was unusual, it did not partake of the nature of breaking bone, but closely resembled tearing fibrous tissue, and was so considered at the time of operation. The tearing sound was communicated to the operator who was holding the pelvis as well as to the one who was manipulating the left leg. It was a diffused sound and its origin could not be located. Twice this occurred, but a third fracture which was found postmortem cannot be accounted for. The bone-ends in all three fractures were in close apposition, clearly indicating that if death had not ensued, repair would have taken place

in favorable position. That no fractures occurred upon the left side is due to the fact that efforts at reduction ceased in about one-half the time spent upon the right leg in realization of the inexpediency of continued efforts. The torn skin over the adductor tendons was accepted as an indication of the low vitality of the patient, as this did not occur in any other case, although several had had ecchymotic spots of quite large size for varying periods of from one to two weeks.

As to the force used it can only be compared with other cases and may be stated as having been skilfully applied and was much less and for a shorter time than in some of the other cases, and especially so in contrast to the fourth patient upon whom Lorenz operated. The forcible manipulations appeared to be suitable to the conditions and there was no recognizable counterindications. The previous condition of the child gave no distinct evidence of her deficient vitality, and it would seem as though the methods employed at reduction were less responsible for the death than the anesthetic, although the entire procedure must be considered.

The pathologic conditions found in the lungs and kidneys, which gave decided indications of very recent origin, could be caused by ether anesthesia for $1\frac{1}{2}$ hours. Pneumonia following ether is sufficiently common in cases in which the operative procedures are of a mild character, and whether acute nephritis is likewise a sequel of ether intoxication is still a disputed point with pathologists, but the evidence in this case is strongly affirmative.

While the condition of the patient did not indicate shock at the cessation of reduction manipulations it was felt that the patient should be most critically safeguarded in every respect. When Dr. Schwartz, the official anesthetizer of the department, was obliged to leave at the beginning of the application of the plaster cast, it was deemed expedient for Dr. Wilson to take his place while Drs. Dolson and Taggart applied the plaster bandages, with Dr. Rugh maintaining correct position of the legs. This disposition of the responsibilities is a satisfaction to all concerned, in that it is believed that everything was done to secure a favorable recovery in this case.

The full details of the postmortem by Dr. Coplin are here given as an essential feature, and their value is enhanced by the disinterested manner in which the report is made, hoping that the conditions, methods,

and results will be of service in guiding others in cases of this kind.

PATHOLOGIC REPORT.

Autopsy protocol, case of B. D., female, 7 years, white. Drs. H. Augustus Wilson and J. T. Rugh, surgeons. Died March 19, 1903, at 9.45 a.m. Autopsy held March 19, 1903, at 1.45 p.m.

Anatomic Diagnosis.—Bilateral congenital dislocation of the hip. Perforate foramen ovale. Persistent thymus. Atheromatous arteritis of aorta and coronary trunks. Acute catarrhal tracheitis. Acute catarrhal bronchitis. Acute catarrhal pneumonia. General tuberculous lymphadenitis. Acute diffuse hemorrhagic nephritis. Latent or obsolescent rachitis.

External Examination.—The body is that of a fairly well-nourished female child. Rigor mortis is quite marked in the upper extremities and the calf muscles, but is slight in the muscles of the thigh. There is marked suggillation on the posterior aspect of the body, neck, head and arms. The thighs are flexed at right angles to the body in the axillary lines, and the legs at right angles to the thighs. The thighs and pelvis are encased in the plaster dressing commonly used after bloodless operation. This is removed in the usual manner, using every precaution to prevent any alteration in the relation of the enclosed parts. In spite of every care there was some movement of the right femur, and it was thought possible that it might have been misplaced, although subsequent findings did not support the view.

From the symphysis to the extreme margin of the right inner condyle of the femur is 24 cm.; on the left side the distance between corresponding points is 32 cm. The circumference of the right thigh, 8 cm. above the inner condyle, is 20 cm.; 22 cm. above the inner condyle it is 29 cm. The circumference of the left thigh, 8 cm. above the inner condyle, is 19 cm.; 22 cm. above the inner condyle is 28 cm. The following external marks are present upon the right inferior extremity: On the inner aspect of the ankle, posterior to the malleolus, are a number of ecchymotic spots, petechial in character, distributed over an area of 4 cm. in the axis of the limb, and 3 cm. transversely. From this point downward the superficial veins are conspicuous, but not palpable, and clearly not thrombosed. Five centimeters above the inner condyle is a pinkish, ecchymotic area 1.7 cm. in length in the axis of the limb, and 5.5 cm. circumferentially. From the lower third of the thigh upward, on the anterior surface, the skin shows pinkish-red mottling almost or quite to the junction of the skin covering the pelvis. This mottling is also present on the inner surface, but less marked posteriorly. Five centimeters from the symphysis, beginning 2 cm. below Poupart's ligament and extending downward, is an abrasion 2.8 cm. in length by 1 cm. in width; 5.5 cm. from the symphysis is a second abrasion nearly parallel with the first, 2.5 cm. in length and 1 cm. in width. At these points the epithelial layers of the skin are stripped and possibly also the connective tissue layers, although the subcutaneous tissues do not protrude or the skin retract; the eroded areas are covered by glazed lymph, through which the ecchymotic bases can be seen. The areas just described are in a larger field of discoloration, greenish-purple with darker purplish mottling, and extending from a point 2.5 cm. to the right of the symphysis to a distance of 15.5 cm. from the symphysis and becoming continuous with the irregular mottling referred to as present in

the lower part of the thigh. The axis of this area corresponds to the course of the femoral artery and the area measures, transversely, 9.5 cm. It extends above Poupart's ligament 3 cm., and from the median line to the anterior superior spine. The skin of the perineum and the cutaneous structures of the vulva are possibly a little redder than normal, while the mucosa of the vulva is suffused with blood and purplish in color, the suffusion being most marked around the urethral orifice. The large area of discoloration already described on the right thigh is soft and almost fluctuating near its center and quite resistant, almost dense at the margin; at the base, near Poupart's ligament, it is quite dense.

Left extremity: Near the ankle are areas of discoloration, petechial hemorrhages and prominent veins essentially of the same kind as described on the opposite limb. On the inner aspect of the leg just within the margin of the tibia is an old ecchymotic patch 7 cm. below the upper end of the tibia. It is purplish with greenish-yellow margins, oval in outline and possesses a maximum diameter of 1.8 cm.; 5.5 cm. above the inner condyle is a pinkish-red area of discoloration, the long axis being transverse to the long axis of the limb, 6 cm. in length and 1.4 cm. in width. Just over the patella is a small ecchymosis 0.7 cm. in diameter. The anterior surface of the thigh shows the same pinkish mottling already described as present on the opposite limb. Four and seven-tenths centimeters to the left of the pubis is an irregular laceration of the epidermis and derma 3.7 cm. in length, 0.4 cm. in width, bridged here and there by fragments of the deeper layers of the skin and margined by smaller fissured lacerations 1 to 2 cm. in length. The long axis of this area is parallel to the axis of the trunk. It is situated near the base of a large purplish-green area, irregular in outline, beginning 3.2 cm. from the symphysis and extending in the axis of the limb 9.5 cm., and in the axis of the trunk 9.5 cm. This area of discoloration extends 2 cm. above Poupart's ligament, at which point it is 4 cm. in length (this latter measurement made parallel with Poupart's ligament). The area is less tense than the corresponding area on the opposite side but similarly colored and with denser margins.

The lower part of the abdomen is flat, or nearly so, the costal margins prominent and the epigastrium slightly bulging. There is a suggestion of a rachitic rosary. The sternal ends of the clavicles are slightly enlarged and the sternoclavicular attachments very relaxed, almost permitting discoloration. The shoulder and wrist-joints, and to a lesser degree, the elbow, knee, and ankle-joints are relaxed; the amount of lateral movement at the wrist and shoulder-joints is strikingly in excess of the normal. The lower end of the radius and tibia (right and left) are apparently enlarged but not conspicuously so. We were not allowed to incise them; they may have been slightly rachitic.

The forehead is prominent, the calvarium large, suggesting the general contour of a slightly hydrocephalic head, the lips are purplish and dry, the pupils are dilated and the eyes slightly sunken.

The axillary, cervical and submaxillary lymph-nodes are notably enlarged; in the axilla nodes possessing diameters of 1.5 cm. can be felt. The anterior cervical nodes are small-r, but distinct chains can be palpated along the posterior borders of the sternocleidomastoid muscle. Under each mandibular angle is located a node approximately 1 cm. in diameter. As none of

these areas was subjected to dissection the measurements given could be estimated only. The tonsils appear slightly enlarged. The oral mucosa is pale but without any discernible lesion.

Internal Examination.—The subcutaneous fat over the chest and abdomen, along the median incision, is scanty but normal in color and texture. The musculature of the chest and abdomen is normal in color and texture, but rather poorly developed.

The peritoneum is normal, the transverse colon considerably distended. There is purplish discoloration of the tissues of all the right half of the pelvis extending down behind the rectum, along the anterior sacral border into the broad ligament, slightly over the posterior part of the bladder and upward anteriorly 4 cm. above Poupart's ligament, corresponding to the already described area of discoloration on the external surface; laterally, on the right side, the purplish shading reaches a point just above the head of the colon. This irregular area of purplish mottling and suffusion is not palpable, although its ecchymotic character is fairly marked. There is slight ecchymosis in the neighborhood of the femoral ring of the left side.

The pleuras are dry, as is the pericardium. Both serosas are normal.

The thymus is exceptionally large, extending anteriorly below the middle of the heart, latterly into the mediastinum, and above to and partly occupying the suprasternal notch. It is an arrow-shaped organ, 9 cm. in length, 5 cm. in width, and 0.7 cm. in thickness. It extends along the trachea as a single body for 1.5 cm., then divides into two equal parts more or less cylindric in outline and 2 cm. in length that are projected upward along the sides of the trachea. Weight, 20 grams.

Histologically,¹ the organ shows no specially noteworthy abnormality. The secondary lobules are much larger than normal in a child of this age. The increased volume seems to depend upon persistence or hyperplasia of the lymphoid elements. The differentiation between periphery and cortex is ill-defined. The bodies of Hassall (concentric corpuscles) are unusually abundant. At a few points rhexis has occurred, and small areas of intercellular hemorrhage, not at any point large or abundant, are occasionally seen. Lipomatous substitution of the adenoid tissue is not at any point in progress. It might be well to note that in many cases persistence of the thymus has been found as a part of the morbid anatomy of rickets.

Heart: The cavities of the right side are distended and occupied by clots, which for the most part are white or the color of chicken fat, with superimposed purplish coagulums. The left side is empty. The valves and orifices of the right and left sides appear normal, except as noted below. The foramen ovale is obliquely patulous, the opening barely transmitting a grooved director. It is 0.3 cm. by 0.25 cm. in size. There is a small patch of atheroma on the ventricular aspect of the anterior leaflet of the mitral. The myocardium is pale, but fairly firm in texture. Weight, 85 grams.

Histologically, the myocardium shows no conspicuous

¹ For convenience in reference the histology of the organ is incorporated with the autopsy record. The technic has been practically the same for all. Selected blocks of tissue were fixed in Bensley's solution, washed, dehydrated, infiltrated with paraffin, sectioned and stained by approved laboratory methods. The findings in each instance are epitomized in this report.

abnormality. Occasional fibers are slightly granular; fat is absent. The smaller coronary branches are not altered.

The presence of even a small atheromatous plaque in the mitral leaflet in one so young indicates the existence of some noxious influence, possibly syphilis, or it may be rickets, as the relatively small heart and thin walled vessels would seem to refute any suggestion that the alteration here noted depended upon heightened vascular stress. The change described below as present in the aorta also supports either of the former views.

The aorta just above the aortic orifice is the seat of a diffuse yellowish infiltration that surrounds the coronary arteries, completely encircling the aorta and has thickened the aorta particularly in the neighborhood of the coronary orifices. The thickening of the aortic wall is at the expense of the lumen. The right coronary artery is surrounded by a distinct zone of such infiltration. Other macroscopic evidence of arterial disease was not found beyond the aorta.

Histologically, longitudinal and transverse sections of the infiltrated aorta show the usual changes of an atheromatous patch. The intima is intact and slightly thickened; the subintimal elastica fragmented at the margin of the area and not demonstrable near its center. The media is partly involved and between the altered media and intima is a necrotic accumulation containing cellular debris, fragments of elastica and granular detritus. Evidences of calcific change are wanting. Sections so oriented as to include the coronary exit show that the process extends but a short distance (1 mm. or 2 mm.) into that vessel. As yet the sectional area of the coronary orifice has not been altered.

Left lung: The superior lobe contains a number of small areas of atelectasis 5 mm. to 10 mm. in diameter, irregular in outline, evidently recent. In the base of the lower lobe anteriorly is a larger, partly collapsed area, not, however, airless, measuring 0.5 cm. by 1.5 cm. The subpleural tissue posteriorly is edematous and the seat of numerous petechial hemorrhages; similar hemorrhages are also present on the diaphragmatic surface and along the anterior margin of the organ. Centrally and toward the upper portion of the lower lobe is a purplish red area 2.5 cm. in length and 1 cm. in width that appears quite airless. Toward the base are numerous smaller areas possessing the same characters. Areas of solidification varying in size from 0.5 cm. to 1 cm. are also present in the upper lobe. Weight, 110 grams.

Right lung: This organ is, in a general way, the seat of changes essentially the same as those noted as present in the left. They are a little more marked posteriorly and less evident at the apex and along the anterior and diaphragmatic aspects. Weight, 125 grams.

The larger bronchi of both organs are the seat of edema and redness of the mucous membrane, and often contain a frothy red mucus.

There is a mucosanguinolent frothy fluid in the trachea.

Histologically, the changes present in the air passages and lungs may be summed up as (1) catarrhal bronchitis, (2) bronchiolitis, (3) lobular pneumonia. None of these is very advanced although all the blocks examined show the changes. The mucosa of the trachea and bronchi, large and small, shows epithelial desquamation, serous and leukocytic infiltration of the submucosa of the large tubes and peribronchial tissues of the smaller. Here and there throughout the sections are

lobules or parts of lobules inundated with mucus or over-distended by compensatory efforts. There is very little interalveolar cellular infiltration.

Properly stained preparations show the presence of an organism possessing the morphology and tinctorial characters of the pneumococcus. The bacteria are not numerically conspicuous although widely distributed.

The peribronchial and mediastinal lymph-nodes, and especially those situated at the bifurcation of the trachea are enlarged and slightly matted together. The larger masses vary in size from 0.5 cm. to 1.5 cm. in diameter, are tense, evidently swollen and, on section, contain greyish dots 1 mm. to 2 mm. in diameter possessing the macroscopic characters of tubercles. The histology of these glands will be given below with other lymphadenoid groups.

The spleen is relatively firm, its pulp of normal density, possibly a little paler than normal. The adenoid groups are not perceptibly changed. Weight, 55 grams.¹

The adrenals are normal in size and general appearance.

The left kidney has retained its fetal lobulation; it is rather hyperemic, soft and cloudy. The cortex is slightly swollen; the labyrinthian areas hyperemic; the malpighian bodies not more evident than usual. The capsule is easily detached; the stripped surface is red and edematous; the redness is rather punctate. The pelvis is normal. Weight, 60 grams.

The right kidney shows essentially the same changes as the left. Weight, 55 grams.

The ureters are normal. The right ureter can be traced downward through the area of hemorrhage; there is no evidence of pressure on it within this area; the mucosa is normal.

Histologically, the kidneys manifest no evidence of any old lesion, but show to a most marked degree the presence of alterations of recent origin. The labyrinthian areas are frequently the seat of irregular intertubular and intratubular hemorrhage. The hemorrhages are recent, the extravasated blood unaltered; tubules are frequently distended with blood-casts. The epithelium of the convoluted tubules is often granular and stains defectively; at no point has it desquamated. The malpighian tufts are frequently engorged, but in exceptional instances only is a tuft found in which free hemorrhage has occurred.

Bladder: With the exception of the subserous suffusion, already mentioned as present under the peritoneal coat, the organ shows no gross lesions. Urethra normal, except at external orifice, as previously described.

The internal and external genitalia show no noteworthy abnormality not already recorded.

The esophagus, stomach and intestines show no important change. The agminated patches are inconspicuous, the solitary follicles prominent. The mucosa of the stomach and lower end of the esophagus show slight erosions thought to be evidences of postmortem digestion.

The pancreas is partly annular, extending about half way round the duodenum. It shows no gross lesion. Weight, 45 grams.

¹Unfortunately the pieces of spleen, adrenal, stomach, duodenum and pancreas were not set aside for histologic study or were mislaid. There is no reason to suppose that a histologic study of any of these organs would throw additional light on the cause of death; possibly it might have shown lesions corroborative of the general condition indicated by what was found in other structures.

Liver: The biliary passages are patulous and normal. The gallbladder lightly distended by apparently normal bile. The superior surface of the right lobe of the liver shows several areas greyish-white in color, irregular in outline, 0.2 cm. to 0.5 cm. in diameter—apparently focal necroses. Posteriorly the organ is lightly congested. There is no special noteworthy lesion.

The mesenteric glands are notably increased in size. Some of the largest are ovoid, measuring 1.5 cm. by 2 cm.; they are fairly numerous at many points, but particularly so in the sigmoid area. They are equally enlarged, though less abundant in the ileocecal region. The enlarged nodules are often tense, the exterior mottled, showing areas of greyish or yellowish-white on a rather pinkish background. The investing peritoneum is smooth and transparent, and the nodes easily freed from the adjacent tissue. On section they are greyish, succulent, and contain minute whitish areas that suggest tubercles; at points there is a suggestion of caseation, but nowhere is this change striking.

The retroperitoneal enlargements are evident, but less abundant. On section these nodes show the same general characters as those in the mesentery.

Macroscopically, the axillary, cervical, submaxillary, mediastinal, peribronchial, mesenteric and retroperitoneal lymph-nodes show essentially the same features. The following histologic description is based on examination of the mesenteric, mediastinal and peribronchial systems.

Histologically, the lymph-nodes manifest those changes characteristic of a moderate degree of widely disseminated infection by the tubercle bacillus. Distinct caseation is scantily present in occasional nodes from all the systems examined; it seems apparent that the peribronchial and mediastinal groups are most involved; they are also the seat of mixed infection. Many nodes are not caseous, nor do they contain macroscopic nor microscopic tubercles, although some of them contain tubercle bacilli. In such nodes the peripheral and follicular sinuses are distended by uninuclear leukocytes and desquamating endothelial cells from the walls; the medullary cords are also closely packed. Occasionally in the peribronchial system fibrin can be demonstrated indicating an acute and active character in the process. In some of these glands pneumococci were identified.

Dissection of the thighs and pelvis: From the median incision two incisions are extended laterally to about the center of Poupart's ligament and then downward on the anterior surface of each thigh following, as nearly as possible, a line parallel with the axis of Scarpa's triangle and extending beyond the area of notable discoloration. Incisions are taken from beneath the deep fascia and finally the arterial and venous trunks partly exposed. Water is forced through the abdominal aorta into each iliac artery until the vessels distend fully. The water oozes from the adjacent infiltrated tissues while the arterial trunks become tense. The veins are similarly tested and with like results. These tests satisfactorily establish that none of the large trunks, or important branches, is lacerated. That the vessels are patulous is also established by opening them at Hunter's canal and observing that the water flows through without obstruction; the thin-walled femoral and iliac veins can be seen to be free from any obstructing or mural thrombus.

The dissection is now extended exposing the muscles of the thigh and finally the hip-joints. The anterior crural nerves and their branches are macroscopically intact. There is considerable difficulty in identifying the various anatomic structure on account of the extensive hemorrhagic infiltration to which the superficial discoloration already described evidently is due. The condition on the right side will be described in detail, followed by an account of the left side.

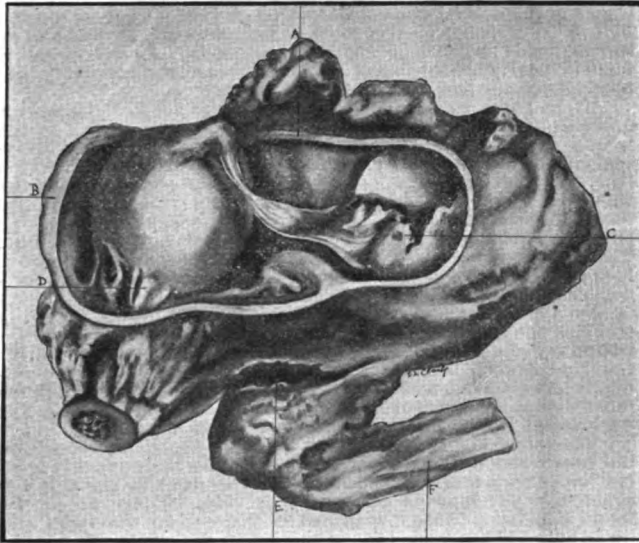
In the cellular and fatty tissue beneath the deep fascia are loculi containing coagulated blood; these small irregular cavities vary in size, the largest scarcely exceeding 1.5 cm. in its maximum diameter. Evidently a number of these spaces may communicate either directly or indirectly. The total amount of blood extravasated cannot be estimated with any degree of accuracy, but is considerable. The distinct cavities containing blood are in the neighborhood of the femoral sheath and beneath the sartorius muscle. (Later a few small loculi were found behind the bone; they were not, however, of notable size.) The inner border of the sartorius and the anterior part of the adductor longus are suffused to a moderate degree. The muscles forming the floor of Scarpa's triangle (iliacus, psoas, pectineus, and, in part, the long and short adductors) are also suffused with blood. The tensor vaginæ femoris and gluteal muscles contain but a few points of interstitial hemorrhage. The intense purplish black staining of the muscles renders it quite impossible to determine accurately just how much, if any, real laceration is present. There are valid objections to complete dissection of the limb, but a fairly exhaustive examination of the exposed muscles fails to disclose any extensive single or massive laceration, although what might be termed a fibrillar dissociation is present in nearly all the dissected muscles already mentioned. The solutions in the continuity of solid muscle bodies are oblique, mixed longitudinal and slightly oblique, but not directly transverse fissurings. The muscles are notably flaccid, probably as a result of post-mortem rigidity and coagulative changes in the extravasated blood.

If there be any laceration of branches of the internal iliac artery a fairly comprehensive examination of the areas in which they are distributed, reinforced by the hydrostatic test already described, fails to disclose it. The intrapelvic suffusion previously mentioned is found on incision to be in the cellular tissue immediately beneath the serosa only, and so far as can be determined, has reached the areas mentioned by infiltration from the neighborhood of the femoral canal.

The hip-joint: The head of the femur seems to be almost in place, but on closer examination, after incision of the capsular ligament, is found to be resting with the margin of the articular surface on the posterior-superior brim of the acetabulum. The head, apparently as a result of fibrous adhesions, cannot be replaced within the joint, although no degree of force was used in the attempt. The capsular ligament and ligamentum teres are relaxed. A slight effort at straightening the limb is followed by the immediate displacement of the head of the femur upward and backward. The innominate bone just back of and above the acetabulum is smooth and seems a little more dense than elsewhere. Realizing that a careful study of the bone and joint at the necropsy would not be possible the ilium was divided just below the inferior curved line and also through the body and ramus of the pubes near the angle and the femur

sectioned just below the trochanter. Recognizing the presence of fractures great care is necessary in removing the specimen and force must be avoided in order to prevent any further alteration in the architecture and relation of the structures to be examined. This specimen was removed to the laboratory and partly dissected by Dr. Aller G. Ellis, who submits the following detailed description:

The specimen as removed consists of those portions of the right innominate bone and upper extremity of the right femur



Right hip-joint. A, thickened capsular ligament. B, capsular ligament at point of maximum thickening. C, ligamentum teres occupying the greater part of the acetabulum; the notable elongation is shown by the relaxed ligament extending to the head of the femur. D, the leader from D is over the line of fracture in the neck of the femur; the point of separation does not show, as it is covered by periosteum. E, fracture of ischium; the periosteum has been divided, showing oblique line of separation. F, second fracture of the ischium; the periosteum is intact and the line of fracture indicated only by the slight darkening due to subperiosteal hemorrhage.

that include all the structures entering into the formation of the right hip-joint. The capsular ligament has been incised along the anterior and superior margin of the acetabulum; it is much thicker posteriorly and externally than below and in front. The acetabulum is slightly flattened, measuring 2.75 cm. in the vertical and 2.25 cm. in the horizontal axis. The greatest depth of the cavity proper is 0.7 cm. The ligamentum teres is 5.5 cm. long, 0.4 cm. wide, and 0.2 cm. thick at its

middle, expanding at both ends. The acetabular insertion is expanded so that it occupies all of the anterior third of the cavity. In addition to this an extension 0.3 cm. thick spreads over about half of the remaining two-thirds of the floor of the acetabulum. The iliofemoral ligament is indistinguishable from the capsular, and the cotyloid and transverse ligaments cannot be exposed without undesirable mutilation of the specimen. The head of the femur is slightly flattened anteroposteriorly. There is a lentil-shaped area of flattening of the articular surface that corresponds to the point of attachment of the ligamentum teres. The ligamentum teres is inserted on the upper portion of an almost plane surface that measures 1.75 cm. by 1.5 cm. This flattened surface corresponds to a similar area on the posterior margin of the acetabulum, the latter area being formed partly of the bony wall of the acetabular cavity and partly by compressed ligamentous tissue.

There is an intracapsular fracture of the neck of the femur. The line of separation passes obliquely across the neck of the bone and at the upper border almost reaches the juxtaepiphyseal line of the head. At the lower border it is 1.5 cm. from that line. The periosteum for some distance on either side of the line of fracture has been separated from the bone by subperiosteal hemorrhage. There is a fracture of the ischium extending through the body of that bone in an almost horizontal plane. The highest point of the line of separation is external where it is approximately 0.5 cm. below the acetabular margin. Subperiosteal hemorrhage is present around this fracture. There is also a second fracture of the ischium passing transversely through the ascending ramus at a point 0.8 cm. above the lower boundary of the obturator foramen. No fragment in any of the fractures shows the slightest displacement; there is no perceptible separation and the slight periosteal hemorrhage is the most conspicuous feature present at the line of separation. The periosteum holds the fragments in accurate apposition.

The left side differs from the right in degree of reposition but in no essential anatomic character. The hemorrhagic infiltration is very much less, but the distribution in the thigh is practically the same as on the other side. There are a few loculi similar to those mentioned as present on the right and distributed along the course of the femoral sheath. The intermuscular and intramuscular suffusion is nothing like so marked as that seen on the opposite side. The head of the femur is scarcely more than raised on the brim of the acetabulum upon which the articular surface rests. The condition of the acetabulum, head of femur and ligaments seems the same as on the opposite side, and a repetition of the description does not seem necessary. There is no noteworthy difference between the periarticular structures on the two sides except that on the left fibrous adhesions are more conspicuous and the head of the bone seems more firmly anchored. This difference is probably due to less thorough dissolution of adhesions possibly originally equally firm on the two sides. No fractures are present on the left side. After section of the almost unresisting muscles it was found almost impossible to place the head of the femur in the acetabulum, although the capsular ligament is opened anteriorly and two fingers placed in the joint as aids to reposition. The resistance to restitution to position seems to be great thickening and dense fibrous adhesions posteriorly; as on the other side, the bulky ligamentum teres occupies the cavity of the acetabulum. No specimen from this side was preserved.

Permission to examine the central nervous system was not obtained.

Bacteriology.—Inoculations on agar and into bouillon were made from the areas of hemorrhagic infiltration and loculi of blood in the thighs, also from the pleuras, pericardium, blood of the heart, spleen, and liver, but no growths were obtained. Tubercle bacilli, as already noted, are present in many of the lymph-nodes, and an organism believed to be the pneumococcus is present in the sections of the lung and peribronchial lymphatics. The last named organism not infrequently fails to develop in cultures made from tissues in which it can be demonstrated by staining methods.

A MUSEUM JAR, WITH IMPROVED DEVICES FOR SEALING AND LABELLING.

BY

W. M. L. COPLIN, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

The basis of this jar is a specimen box manufactured by Fettke and Ziegler, of Germany, and in this country supplied by a number of importers. The jar is as nearly rectangular as it is possible to manufacture it, and, if desired, may be purchased with one side ground and polished.

Nearly two years ago we started the use of these jars for mounting museum preparations, and found great difficulty in maintaining a satisfactory seal. The glass lid can be attached water-tight by means of paraffin, paraffin and beeswax, or by various cements. Our experience with the cements has not been encouraging. Asphaltum and gold size have yielded fairly satisfactory results; putty has been recommended. Sometimes, after sealing, the fluid becomes cloudy, and the greatest difficulty is found in breaking the seal and changing the fluid. If the cement has been satisfactory, it is almost impossible to clean it off and secure accurate coaptation and seal, while with the less efficient cements, that can be removed easily, one almost never secures a water-tight joint.

For the purpose of overcoming some of the difficulties indicated above, the clamp shown has been devised. It consists of two plates of lacquered brass reinforced at the top with ribs to prevent bending, and joined on the sides by lacquered brass rods 0.5 cm. in diameter. The rods are secured to the bottom plate and

passed through the top plate, which is fastened by milled-head nuts applied over the projecting ends of the rods. The jar at the bottom is protected from contact with the brass by a thick rubber cushion, and a second cushion is applied between the glass lid and the jar, and a thick rubber cushion between the top of the glass lid and the bottom of the top plate of brass. These rubber sheets are for the purpose of cushioning against expansion and contraction in response to temperature changes. The brass plates are rectangular, permitting the jars to be placed upon the side or upon edge as well as on end.

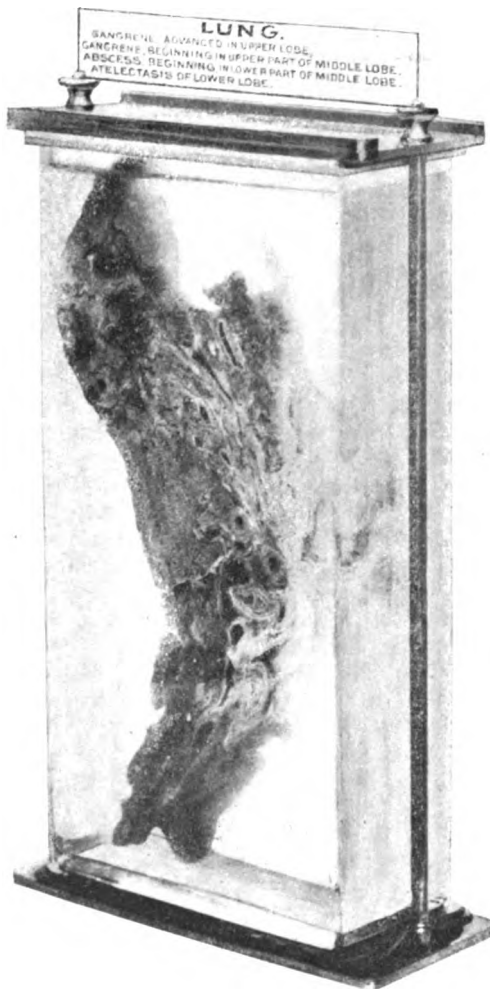
An additional feature is the device for labelling. Everyone knows that on jars used for museum mounting, and especially where they are handled by students, labels become soiled or illegible, and often detached. Attempt has been made to overcome this difficulty by utilizing cards of the same size (12.5 by 7.8 cm.) as those used in the ordinary card index. The card used for labelling is secured above the top plate by slits in the projecting ends of the vertical rods; it may have written or printed matter on both sides.

The specimens mounted in the jars exhibited have been in position for several weeks, during which time the seal has remained perfect, although one of the jars has been carried from place to place in a handbag.

In one of the jars is shown a glass frame for retaining the specimen in position. This frame is easily made from a glass rod, and is especially valuable for exhibiting specimens not possessing sufficient volume to retain their shape; pieces of intestine, serous membrane, and the thin walls of cysts may require such supports. As a rule, however, such devices are unnecessary. The approximate inside dimensions of the finished jar are: height, 20 cm.; width, 9.5 cm.; thickness, 4.5 cm.

I am indebted to Queen & Co., of this city, for the experimentation that was necessary in the evolution of the details of this jar, and also for the accompanying illustration.

March 12, 1903.



Museum jar, with improved devices for sealing and labelling. (The ends of the vertical rods project very much more than is indicated in the cut, and hold the card firmly.)

BRANCHIAL CYSTS AND FISTULAE*

By W. M. L. COPLIN, M.D.,

of Philadelphia.

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As a result of the complex developmental processes requisite to the formation of the organs arising in the neck segment of the embryo a multitude of malformations are rendered possible. The formation of the branchial arches and associated clefts or more properly furrows, and the fact that, at the bottom of the furrows, internally as well as externally, the epithelium of the endoderm and ectoderm becomes contiguous, considered with possible errors at the anterior median junction of the projected developing columns, such as failure of median coalescence, render it at once apparent that all sorts of malformations or arrests in development may result. Such more or less complete persistence into extrauterine life of conditions normally entirely fetal may be manifested by almost any degree of abnormality from fissure of the entire neck to trivial fistulae, or from absence of more or less of the esophagus, lung, or other structure normally derived from the foregut, to the persistence of fistulae (often of capillary dimension†), blind sacs or cyst accumulations due to external and internal closure of canals without coalescence of intermediate tracts. I shall not attempt to go into the developmental processes concerned in the formation of the branchial clefts, as such information is attainable in any of the current works on embryology.

Hunezowski¹ (1789) reported two cases of congenital cervical fistulae; Dzondi² (1829) called them tracheal fistulae and Ascherson³ demonstrated their pharyngeal connection. Heusinger⁴ reported 2 cases and gave a

* Read before the Philadelphia Pathological Society, January 10, 1901.

† In one of Heusinger's cases a thick whisker could be passed into the opening.

table of cases, 46. In his inaugural thesis (Paris, 1877) and later, Cusset⁸ gives with considerable detail the result of his studies on the subject. Guzman's⁹ thesis in 1886, and Bland Sutton's⁷ work on tumors should also be consulted. Senn⁶ discusses branchial cysts under teratomata. Recently Frederick Shimanck⁵ reported cases of branchiogenic carcinoma and reviewed the literature of malignant disease, arising in these abnormal cavities.

With regard to the classification of branchial cysts much diversity of opinion is found. Fevrier¹⁰ speaks of median and lateral cysts. Depending upon their proximity to the surface the cysts are spoken of as superficial or deep. As it is not always possible to determine accurately from which cleft the cyst originated the proposition to base the classification upon the embryologic origin of the defect can be scarcely regarded as satisfactory. Less satisfactory probably is the attempt to subdivide these cysts according to the contents, as the latter must be materially influenced by the presence of inflammation, hemorrhage, and infection, as well as its source; similarly situated and genetically identical cysts may contain dissimilar materials.

Based, however, upon the hypothesis that such a classification is justifiable such cysts have been called atheromatous (branchial dermoids), mucous, serous, and hematomas. As none of these cysts are primarily blood-cysts it is probable that the last-named subdivision is hardly justifiable. In Marsh's¹¹ case the cyst contained a gelatinous material.

It has been proposed to name these cysts according to their anatomic position in the adult. From this point of view such cysts are called auricular or auditory, parotid, submaxillary, sublingual, pharyngeal, tracheal, etc. If carried to its legitimate conclusion such a classification would be scarcely consistent, as we would have substernal, sternocleidomastoid and other anatomic subdivisions that would endanger our losing sight of the embryologic origin. Although possessing many disadvantages the classification based upon the character of the cyst wall, taken in connection with the origin of the process, possesses many advantages. This would at once subdivide the entire group into two subgroups, one in which the wall showed to a varying

degree the histologic characters of the skin and which would merit the name branchial dermoid, and the other in which the epithelial lining showed more or less striking resemblance to the mucosa lining the mouth, pharynx, or respiratory tract. Cysts of the latter type would be called mucous branchial cysts. While considering the subject of classification it is well to remember that the branchial cyst is but one type of a malformation that may be manifested by at least four pathologic possibilities: 1. Branchial fistulae, canals extending from the external surface to one of the mucomembranous tubes or cavities, such as the pharynx, larynx, etc. 2. Where the external opening has been closed a blind fistula, pouch or tract with its internal opening retained, results. 3. An external fistula in which the pharyngeal, laryngeal or other internal orifice has been closed while the external opening persists. 4. Cysts like that observed in the case reported in which both internal and external orifices have been obliterated, giving rise to a closed cavity the wall of which possesses an epithelial covering. In the experience of Trelat¹² fistulous openings are seven times as common as true cysts.

As already indicated the structure of the wall depends to a certain extent upon the type of tissue that it imitates. In branchial cysts of the dermoid type the wall does not differ from that found in other dermoids except from the almost constant presence of lymphoid elements in the extradermal layer. This lymphoid layer may be scanty, consisting of a few aggregations of lymphoid cells scattered here and there or such agminations of lymphoid tissue as to constitute distinct nodes. While it is true that other dermoids may occasionally possess more or less lymphoid tissue it is very rare to find such accumulated masses as are observed in the dermoids of the type at present under consideration. In the branchial cysts imitating the mucous membrane in the character of the cyst wall the condition is practically always that observed in the case here reported. In a small number of cases the lining has been composed of cylindrical epithelium, rarely of the tall variety, and only exceptionally ciliated. Where the epithelium has been subjected to considerable in-

ternal pressure it may be flattened, of a low columnar (cuboidal) type, or less frequently quite resembling squamous epithelium. In only exceptional instances is it simple, usually stratified, the number of layers not uniform in different areas of the same cyst wall and not infrequently showing marked morphologic peculiarities in different areas of the same lining. When stratified the genetic layer shows more or less tendency toward a distinctly columnar type. It is not probable that epithelium is ever absent, and the only reported case that I have been able to find in which it was sought and not found is that recorded by G. Broesike,¹³ but as the specimen was not studied in the fresh condition the absence of demonstrable epithelium is not surprising. The muscularis mucosa may be demonstrated with difficulty or it may be on the other hand quite conspicuous. Sometimes it is composed of a scattered layer of smooth muscle cells, abundant at points, irregularly scant in other areas, and rarely arranged as a continuous membrane. Sometimes this layer is in immediate apposition with a firm connective tissue stratum composed of fully formed fibrous tissue in which may be found numerous leukocytes, usually of the lymphoid type. This fibrous tissue merges into the loose connective tissue by which the cyst is attached to neighboring structures. Elastic fibers are present in the case reported. Adjacent to the fibrous tissue and, when it is absent, adjacent to the muscularis mucosa could be found a varying amount of lymphoid tissue. Sometimes this lymphoid tissue is in type and arrangement a more or less accurate reproduction of the structure of the tonsil. In other instances there is a lawless aggregation of lymphoid elements with a scant reticulum scattered along the submucosa at irregular intervals and in various sized aggregations.

A number of observers, Cusset,⁵ Roth,¹⁴ Monad and Dubar,¹⁵ and Guzman,⁶ have called attention to the presence of glands in the walls of branchial cysts. These glands may be of the serous or mucous type and show such aggregations as are found in the pharynx and esophagus of lower animals, and though less abundant in man; such glands may be distended by secretion, constituting true cysts in the primary cyst wall,

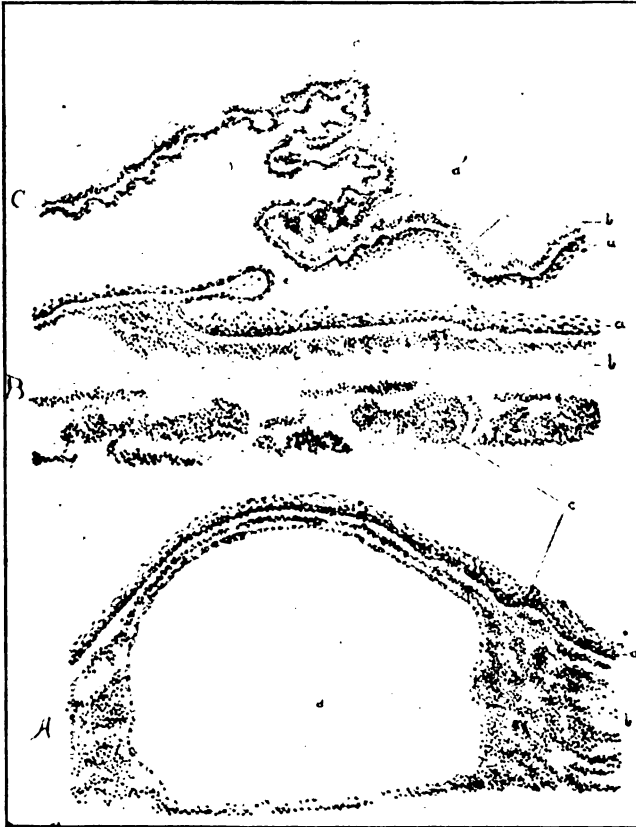
or possess patulous ducts communicating with the general cyst cavity. Commonly the glands are not abundant and apparently may be absent or overlooked. The cyst wall may be uniform and quite smooth or it may be irregular, as in the case reported, of varying thickness depending upon the amount of lymphoid and fibrous tissues rather than upon the thickness of the epithelial layers.

Sometimes the cyst extends in finger-like projections between the muscles, great vessels, and nerves of the neck, or behind the hyoid bone, or downward behind the sternum or along the course of the auditory canal, rendering total ablation sometimes quite difficult, if not impossible. Sometimes the tumor projects into the pharynx or esophagus or passes posteriorly to that structure or between the esophagus and trachea or larynx, and while presenting superficially as a rather simple and readily accessible mass it may at operation present unexpected difficulties.

The communication of blind or open fistulae with the air-passages may give rise to air-sacs; those sacs possessing internal openings into the trachea may present the features of that rare condition variously termed aerial goiter, aerial bronchocele, tracheocele and hernia of the trachea. Stuart Eldridge¹⁸ reported one such case and collected the literature bearing upon the subject. I gather from a perusal of his paper that he believed it quite possible for the defect to be latent, a mere point of weakness, which, under unusual stress, became manifest.

With regard to the symptoms of this condition little need be said, as they suggest themselves. The external opening of fistulous tracts may be situated almost anywhere in the anterior portion of the neck, about the auditory canals, in the temple, in the neighborhood of the jaws, etc., but always anterior to the sternocleidomastoid muscles. The external opening is commonly marked by a discoid area of scar tissue or sometimes it may be so inconspicuous as to escape superficial examination. Only rarely can the fistulous tract be followed by a probe. Fevrier¹⁹ reports the occurrence of severe reflex symptoms—pallor, palpitation of the heart—as a result of attempted exploration of a pharyngeal fistula.

The discharge is usually clear mucus, but may be mistaken for salivary secretion from which it is easily differentiated by the usual chemical methods.



- A.** Section from thick portion of wall of branchial cyst. This section is richest in lymphoid tissue and shows the presence of the cyst *d*, containing granular detritus and lined by modified low columnar epithelium.
- B.** Section of wall of branchial cyst at point where thicker portion is thinning toward the extremely thin layer shown at *C*. Sections *A* and *B* are placed with the inner aspect of the cyst wall directed upwards.
- C.** The section is reversed, the inner aspect being directed downward. *a. a. a.* Epithelial layer of cyst wall. *b. b. b.* connective tissue layer. *c. c.* lymphoid elements in cyst wall. At *d'* these lymphoid elements are aggregated in masses resembling the tonsil in structure. *e.* Section of one of the folds observed in the cyst wall. *f.* Irregularly dilated gland ducts. Tissue fixed in Heidenhain's solution, infiltrated with paraffin, stained with carmalum and picric acid. Zeiss 8 mm. Apoch. Projection eyepiece No. 2.

Where the fistula is complete and communicates with the esophagus or pharynx droplets of milk may escape during deglutition.⁷ The location of the external opening is rarely a guide to the extent and relations of the fistulous tract or sac. Stimulation of salivary secretion by citric acid or mastication usually stimulates the secretion from the sinus even when it does not communicate with the alimentary canal.

When opening internally without an external opening the condition is commonly spoken of as a pouch or diverticulum (congenital);* when communicating with the esophagus it may fill during feeding or the internal opening may be so small as not to admit food. It may be evacuated by pressure, or the patient may find that by assuming a certain position the food does not enter the diverticulum.

Like the fistulae the cysts are, in the neck, located anteriorly to the sternocleidomastoid, in the parotid or auricular region, in the neighborhood of the hyoid bone, or maxilla, in the interclavicular notch, or less commonly substernal, presenting at the last-named point.

The character of the contents has already been considered. The striking resemblance in some cases to pus or to the caseous contents of tuberculous lesions may mislead the operator; as indicated in the report which follows it would seem that the character of the cells found in the fluid should at once clear up the diagnosis.

With regard to the age at which the lesions manifest themselves it may be said that the fistulae are usually present at birth. They may appear later as a result of opening of pouches or cysts or incomplete extirpation. Like dermoids of other kinds the cyst may escape detection until adult life or later. In Cussett's⁶ cases the patients were 10, 15, 21, 22, and 26 years of age. In the case reported the specimen was sent to the laboratory by Professor W. W. Keen, to whom I am indebted for the following clinical notes:

C. E., age 36, first consulted me November 6, 1899, at the instance of Dr. C. W. Richardson, of Washington, D. C. His father and mother are living, and in good health. Of

* For description of dissection see references Nos. 12, 13, and 16.

his grandparents he knows nothing, except that his paternal grandmother died of old age at about 85; he believes that all of his family were healthy. One sister died of diphtheria. Three years ago he noticed a lump on the lower jaw on the left side, no pain, no inflammation, in fact no symptoms whatever. Its size was that of a peach stone until about 8 months ago, when it began to grow quite rapidly. There have been, however, no symptoms connected with it, excepting a slight, dull pain about the side of his face, and he thinks it has affected his head, as he has become very forgetful. He has lost 28 pounds in the last 6 months, weighing at present 175 pounds, but this may be due to other causes. On examination I found a soft, almost fluctuating tumor, 10 by 6 cm., presenting the features of a lipoma.

Operation, November 15. An incision was made parallel with the jaw, and after cutting down through the mylohyoid the back of the tumor was reached. This proved not to be a fatty, but a cystic tumor. The fluid looked very much like pus. My judgment was that it was a cold abscess either in the connective tissue or in a very much enlarged and softened gland. I was able to dissect the whole of it out, exposing at the bottom of the wound the great vessels of the neck. I very carefully washed the wound out with salt-solution, and then closed it with drainage. He made a perfectly smooth recovery, highest temperature being 100° F.

Pathologic Report—Specimen, cystic tumor of neck. Specimen consists of an almost empty, flaccid sac, measuring 7 cm. in its longest diameter. It is oval or slightly pear-shaped. It contains a pinkish-white opaque fluid that resembles pus. The external wall of the cyst is covered by an aborescent outline of bloodvessels. The lines of dissection from the adjacent tissues are recognizable. By reason of perforations in its wall it was impossible to refill the cavity and determine its capacity. Approximately one-half the cyst wall is thin (1 to 2 mm.) perfectly transparent, and containing a few bloodvessels. The remainder of the wall is thicker, but quite irregular in thickness. Its maximum thickness occurs in slightly bossed elevations approaching 1 cm. The average thickness of the wall does not exceed .25 cm. It is irregularly studded by greyish translucent elevations. The largest of these elevations are palpable, resembling tubercles. At one point in the thickened wall is a yellowish mass apparently caseous. This mass is ovoid, .7 cm. by .5 cm. in diameter. It is situated within the thickened wall and covered by a thin layer of tissue. At other points the cyst-wall is traversed by thin septa, dividing it into irregular depressions. In a general way the color is pinkish with areas of what appears to be hemorrhage, some of which are purplish. At some points the wall is fibrous and very dense, in other areas it is soft and yielding. Weight 17 gms.

Fluid contents of the cyst : The quantity is insufficient to determine the specific gravity. The cells vary in size and contour in the size of the nucleus and in the quantity of perinuclear protoplasm. The best picture of these cells is obtained in spreads, dried, fixed by heat, and stained in hematoxylin and eosin, toluidin-blue and eosin, and Unna's polychrome methylene-blue.

1. The most abundant cell observed in such preparations is of relatively large structure, varying in size from 12 or 15 μ to 35 or 40 μ . In shape these cells are irregularly oval, a few are round or discoid, while by far the large part are irregularly polyhedral. The majority of these cells are mononuclear; occasionally, a cell is to be found containing two nuclei, and in very rare instances three distinct nuclei can be recognized. Some of the nuclei, indeed one may say the majority, are in a fair state of preservation. Nuclear fragmentation, fissuring, vacuolization and polychrome reactions are recognized. In some of the cells a distinct nuclear structure is no longer to be recognized. In others the nuclear remains are but faintly tinted, constituting irregular shadows in the cellular protoplasm, while in still others the chromatin is fragmented into irregularly outlined granules which stain unevenly. In many of the cells the nuclear margins are indistinct. The perinuclear protoplasm is, for the most part, finely granular, and takes the acid stain with varying degrees of intensity. Its volume varies within wide limits : the different-sized cells owe their differences in size to variations in the quantity of protoplasm rather than to any variation in size of the nucleus, which is rather uniform. There are apparently free nuclei which probably belong to these cells as indicated by the irregular, ragged rim of protoplasm which stains unevenly and often but slightly. The protoplasm is vacuolated in many of the cells, the vacuoles varying in size from 1 or 2 μ to 7 or 8 μ . In some of the cells of this group, the margin is fairly regular and clearly defined. In others, the margin is ragged but sharply outlined, while in still others the protoplasm fades off, and is gradually lost without any sharply outlined limit.

2. An occasional finely granular oxyphile leukocyte can be recognized, although the number of such cells is remarkably small.

3. Occasionally one finds a cell morphologically and tinctorially like a mononuclear leukocyte. These cells, however, are not abundant. There are a few masses of cells, in which distinct differentiation cannot be made out, and within these might be included other cells than those described. A few erythrocytes are present.

A count of a thousand cells in spreads made from the fluid gives the following result in percentages :

1. The large cells resembling the squamous epithelial cells described above, 93.7 %.

2. Finely granular oxyphile leukocytes (polymorphonuclear leukocytes), 1.8 %.

3. Erythrocytes, .5 %.

4. Uninuclear leukocytes and unidentified cells, 4 %.

Portions of the cyst wall at various points were fixed in Heidenhain's solution, infiltrated with paraffin, sectioned, and sections stained with carmalum alone and with picric acid, hematoxylin alone and with eosin, Unna's acid orcein, Unna's polychrome methylene-blue, toluidin-blue alone and with eosin, toluidin blue with differentiation in styron and glycerin-ether, and by Gram's method, and for tubercle bacilli with carbol-fuchsin.

For convenience in description, and for the sake of brevity, the sections from the following areas will be considered :

A. Sections from the thin part of the wall. B. Sections from the thicker areas.

A. The best sections from this part of the wall are in the neighborhood of areas where the thin wall is suddenly or gradually converted into a thick wall by changes which will be mentioned later.

The inner aspect of the wall is lined by large polygonal cells, evidently epithelial. Toward the free margin the cell outlines are not distinct, the nuclear stain is not strong, and vacuoles are abundant in the perinuclear protoplasm, which, under a very high power, is slightly granular; although it is impossible to give accurately the thickness of this layer (which varies) as it merges gradually with the cells below, it may be stated that it approximates two or three of the cell-layers. Just under this layer the irregular polygonal cells become more sharply defined both in outline and

stain reaction. Toward the upper layer already described, the nuclei are less distinct, becoming more and more clearly defined, and stained with greater intensity as we approach the subepithelial layer. The germinal or basement layer of epithelium is irregularly columnar, with deeply stained nuclei, in some of which changes suggestive of karyokinesis are to be recognized. From this layer passing upward can be recognized the gradual transition from the irregularly columnar form to the more or less flattened, irregular, and poorly stained cells already described as present upon the free surface.

As indicated by the above description the epithelium of the wall cannot be divided into distinct layers, although there is the suggestion of a stratum corneum and stratum Malpighii. A distinct muscularis cannot be recognized in sections stained in the usual nuclear dyes, although here and there a few long spindle-shaped cells with rodlike nuclei are to be recognized. In sections stained in acid orcein a delicate basement membrane can be recognized at nearly all points; this structure sends trabeculae downward in many areas, penetrating the lymphoid tissue below. While the stratum germinativum is slightly irregular one cannot say that there is anything more than a mere suggestion of papillae. Immediately under the epithelial layer described one finds nearly the whole length of the section a slightly irregular layer of lymphoid tissue. The reticulum varies in quantity, being at some points rather abundant and at other areas scanty. It is not rich in bloodvessels, particularly toward the epithelial surface; as we approach the outer limits more vessels are to be recognized. The cells occupying the reticular spaces correspond for the most part with the usual type of lymphoid cell, and scarcely merit further description. A few finely granular oxyphile leukocytes are present, although there is certainly no excess of these elements. At points the outer wall, or I might better say outer limit of the wall, is formed by lymphoid tissue. In other areas it is formed by masses of fibrillated connective tissue comparatively rich in bloodvessels and containing a few unstriped muscle fibers. The roughened and irregular free margin at this point is, of course, due to its dissection from adjacent tissue. I have not

been able to demonstrate the presence of striped muscle-fibers in this area.

B. Sections from Thicker Areas in the Wall.—As the increased thickness of the wall in different areas is due to different causes it would be necessary to consider these areas separately.

1. Areas in which the thickening is due to a thicker wall of lymphoid tissue. The epithelial covering in these areas deserves no special description, as it varies little if at all from the epithelial layer seen in the thinner wall. Partly as a result of its increased thickening and possibly from other causes, the cellular elements usually present on the mucous surface can be more readily recognized, although, as is usual under such circumstances, differentiation into layers is not clear. Cross-sections of flattened cells, such as those already described as present in the fluid contents of the cyst, with flattening, or slight elongation of their nuclei, are to be recognized. There is the same gradual transition from the irregularly columnar germinal layer to the flattened surface layer already described. In some of the thicker areas the lymphoid tissue is more abundant and the reticulum scanty. In other areas the reticulum is more abundant, with a suggestion of proliferative change and corresponding reduction in the richness of lymphoid cells. Distinct arrangement of cells such as compose adenoid follicles of a lymphatic gland can be recognized, and occasionally there is a suggestion of medullary cords, although demonstration of these structures is not complete. External to the lymphoid areas just described there is the same area of fibrillated tissue containing a few long, spindle-shaped cells with rodlike nuclei. A further study of these lymphoid masses reveals the presence of necrotic spots. Such points embrace only a few cells. Just beneath the germinal layer in some of the sections there is a lymphoid infiltration of the connective tissue not associated, however, with the presence of finely granular oxyphile leukocytes. These bodies are not abundant at any point in the section.

2. Areas in which the increased thickening of the wall is due to the presence of cysts. The epithelial covering in these areas merits no further consideration than that already given. Only one of these cysts will

be described. In designating this distinctly as an additional cyst, the possibility of its communicating at some points with the larger cysts cannot be overlooked, although such communication cannot be demonstrated even in serial sections. The wall of this cyst is formed by an inner zone of squamous epithelium which has been detached or has disappeared from some areas. It shows the same general appearance as that already given for the epithelial lining of the larger cyst. At one point the two cavities are separated by a thin wall less than 1 mm. in thickness composed of two epithelial surfaces between which is a small quantity of fibrillated tissue rich at points in lymphoid cells.

Macroscopically on section this cyst possesses a diameter of .3 cm. and corresponds with what was mentioned in the gross description as a distinctly yellowish mass measuring .7 by .5 cm. The difference between the diameter in the gross specimen and the section is probably to be attributed to shrinking and the removal of fluid from the interior of the cyst or to the section not passing through the greatest diameter. The cyst contents as examined in the fixed and infiltrated preparation are usually composed of fine, intensely acidophilic granules resembling in many respects the detritus in caseous areas. That it is not caseous in the true sense is shown by the fact that it contains large squamous epithelial cells such as have been identified in the fluid from the larger cyst. Most of these cells have lost their characteristic stain reaction, selecting only the acid dye and therefore possessing indistinct, irregularly defined nuclei and cell outlines.

The contents as here studied must be considered to be the product of degenerative changes in the epithelium which has been cast off into the cyst cavity. Three smaller cysts identical in all their essentials with that just described have been found, and it is reasonable to infer that the many small whitish or greyish, translucent elevations mentioned in the gross description were probably, or at least some of them, cysts resembling the one just described.

3. Sections from other areas in the cyst wall show evidences of chronic inflammation manifested by a lymphoid and plasma cell infiltration with the produc-

tion of fibroblasts, and in some areas cicatricial tissue. At a few points the mucosa shows distinct papillae. They are, however, not abundant. Occasionally there is a distinct fold resembling the irregularities or rugae observed in mucosae surrounding cavities whose walls possess considerable distensibility. Transverse section of the overhanging rugae gives the appearance, at times, of superficial gland-like projections. Serial sections, however, show clearly that these are folds. In other areas distinct glands are demonstrable and it is evident that the cysts already described have resulted from distention of gland acini, or ducts, or both.

Bacteriology.—Cultures were not obtained from the cyst contents. Spreads and sections show the presence of a few cocci in the cyst contents and in the wall; these cocci stain by Gram's method, are apparently staphylococci, few in number, and the absence of cellular infiltration as well as the scant necrosis would indicate that the infection, if such existed at the time of extirpation, is inconsequential.

Diagnosis and Remarks.—There can be no doubt of the branchial origin of this cyst. The character of the epithelial covering, its arrangement, the morphology of its cells, the structure of the submucosa, the presence of cysts in the wall, the abundant lymphoid tissue and the cyst contents all point to the branchial origin. From a practical view the character of the cells found in the fluid contained within the cyst offers important diagnostic aid. The small number of leukocytes of the type usually found in pus and the presence of large mononuclear cells rich in perinuclear protoplasm, and the absence of necrotic material should be in the future of value in diagnosis. In cysts of endothelial origin, similarly located, it is not likely that exfoliated cells would ever present the morphologic and tinctorial characters recognized in the case reported. Endothelial cysts possessing richly cellular fluid contents would, no doubt, owe their cellular elements to the presence of migrated leukocytes and exfoliated endothelium, in which case no such a cell count as that reported would be found. It would therefore appear to the writer that an examination of the fluid that came from such a cyst, taken in consideration with its location and clinical

history should make the diagnosis less difficult than it at first appears.

With regard to the treatment little need be said; total ablation, where possible, is the only commendable plan. Pockets that cannot be excised may be cauterized. Poncet¹² used chlorid of zinc but does not give the strength of the solution used; tincture of iodine, carbolic acid or the actual cautery may be used. All surgeons are agreed that the use of irritants and escharotics, either by injection or application with a swab, is untrustworthy.

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A BRANCHIAL CYST, THE WALL OF WHICH CONTAINED A SMALL HEMANGIOMA.

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CLINICAL HISTORY.

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It is not our purpose to discuss the pathology of branchial cysts as this has been dealt with in an article by one of us¹ elsewhere. We desire to place on record what appears to be an unique case of which the following are the essential facts:—

Clinical history.—J. P., a lad of 17, with a negative family history, came to the Jefferson Hospital for treatment. He stated that, when he was 20 months old, a pimple was first noticed in the region above the pomum Adami, which would close at times and then collect and discharge a mucopurulent material. This condition continued until he was about 15, when the swelling was lanced. A partial improvement resulted, but the previous condition returned in an aggravated form. About this time or two years ago, he stated that it was cauterized, and subsequently entirely healed. A sense of fullness soon after developed at the site of operation; when pressure was made upon this point something would flow into his throat, and after a severe coughing spell would be expectorated. The material resembled that formerly discharged anteriorly.

Examination showed a firm cicatrix in the mid-line between the hyoid bone and the thyroid cartilage, somewhat bulging, with a slight fluctuation. Pharyngeal examination was negative. A diagnosis of branchial cyst was made and he was admitted for operation. A general anæsthetic was given, and a longitudinal incision made through the scar tissue. About 2 cc. of mucus was evacuated, and a probe led only to the hyoid bone. The sinus was dissected

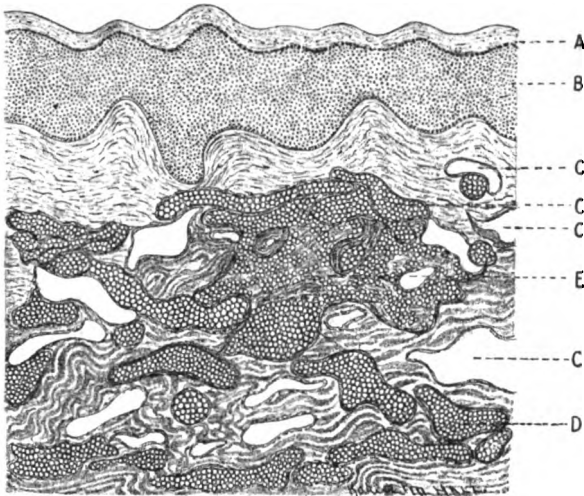
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out and freed from its hyoid attachment, the probe could now be passed upward toward the floor of the mouth, but did not penetrate the oral mucous membrane. The sinus was entirely removed and careful search instituted for a communication with the pharynx, but none could be found. The wound healed nicely, but, about a week later, a small amount of mucus was again discharged, which was repeated in smaller quantity at intervals of 3 or 4 days.

At the last visit no discharge had taken place for a week, and since the last operation there has been no flow into the pharynx. Repeated examinations have failed to show any opening into the mouth or pharynx.

Pathological Report.—Specimen consists of a small piece of tissue 0.8 cm. in length and 0.4 cm. in width; weight 0.4 gm. It is rather firm in consistency and pinkish red in color. One surface is wrinkled, the other is rough and studded by shreds of tissue; this surface has evidently been dissected from other structures. The specimen was fixed in Heidenhain's solution, embedded in paraffin, sectioned and the sections stained with hematoxylin, eosin, picric acid and by Van Gieson's method for connective tissue.

Histology.—As may be judged by the size of the gross specimen, sections made at right angles to the long axis are small and fragmentary, rarely exceeding 0.4 cm. in the longest diameter. One surface possesses an epithelial investment consisting of stratified epithelium of the squamous type; from 6 to 10 cell layers can be recognized. These show a more or less perfect separation into at least three distinct strata, which occasionally blend. The most superficial layer corresponds to and possesses the general histologic characters of the corneous layer of the skin. On section the superficial stratum is composed of thin irregular strands, presumably the sides of flattened squamous cells entering into the formation of this layer. The surface is rarely smooth, being both papillated and roughened by projecting cells or strands, the free ends of the latter hanging from the attached layer. The stratum yields the usual microchemical reactions of elements rich in keratin. It joins rather sharply with the underlying cellular stratum—a layer possessing the cellular elements normally present in the rete Malpighii of the skin. The outer layer is formed of cells that on section are spindle-shaped, the long axis of the spindle being parallel to the surface. This stratum stains indifferently, contains a few intra- and intercellular granules and shows the microchemical changes commonly present at this point. Immediately beneath the cells just described are larger and more fully formed, morphologically perfect cells of the squamous variety resembling those of the deeper part of the normal rete Malpighii. Cells with protoplasmic bridges (prickle cells) occur but are not abundant. Just beneath this layer is an irregular rather



- A. Corneus stratum.
- B. Malpighian stratum.
- C. Caverns, the contained blood cells of which have not been represented in the drawing; 14 of these spaces are present.
- D. Caverns containing blood cells.
- E. Area in which hemorrhage has occurred in hyalin matrix.

poorly outlined, and indifferently staining genetic layer, the cells of which do not assume the columnar type usually observed. They are polygonal, cuboidal and, though rarely, of the taller columnar type.

The epithelial layers just described rest upon a thin connective tissue stratum that merits no further description than that indicated by noting its strong resemblance to the corium. It possesses the usual papillary projections and corresponding depressions accurately fitted to the overlying epithelium. The vascular loops in the papillæ are sometimes surrounded by lymphoid cells but on the whole the layer is quite free from cells. It is usually coarsely fibrillated but at many points it is homogeneous—hyaline. It rests loosely upon the adjacent connective tissue which contains numerous bloodvessels, usually thick walled; an occasional hair follicle is present in this layer. At one end of the section situated just under the corium, which is not invaded, is the most interesting feature of the specimen, namely a somewhat imperfectly formed but still clearly outlined angioma of the cavernous type. The bloodspaces

are filled with erythrocytes and the enclosing walls formed by hyaline almost homogeneous fibrous tissue. At first glance this mass of blood was mistaken for an area of ecchymosis, but close inspection showed that while at many points the blood is free in the connective tissue, in still other areas distinct walls and uniform caverns can be made out. On the wall of some of the caverns a distinct endothelial lining can be recognized. The angiomatous area is rather clearly outlined, but not encapsulated. The vessels of the subcutaneous tissue adjacent to the angioma are larger than normal, but not conspicuously so.

Diagnosis and remarks:—The cyst is clearly of branchial or thyroglossal origin, and possesses the histological elements in its wall already mentioned to justify its being designated a *branchial dermoid*; the only unique feature is the presence of an angioma in its wall. Both processes are of congenital origin and constitute developmental defects. Neither is uncommon, but so far as we have been able to find the coincidence of angioma and branchial cyst is here recorded for the first time.

A CASE OF CONGENITAL HEART DISEASE.*

BY EDWIN E. GRAHAM, M.D.,

WITH REPORT OF AUTOPSY

BY RANDLE C. ROSENBERGER, M.D.,†

Philadelphia.

C. L., aged one year. Admitted to Jefferson Hospital November 18, 1901.

FAMILY HISTORY.—Father and mother are living and well. A maternal aunt died of phthisis. There was no other history of tuberculosis, nor of any malignant disease obtained.

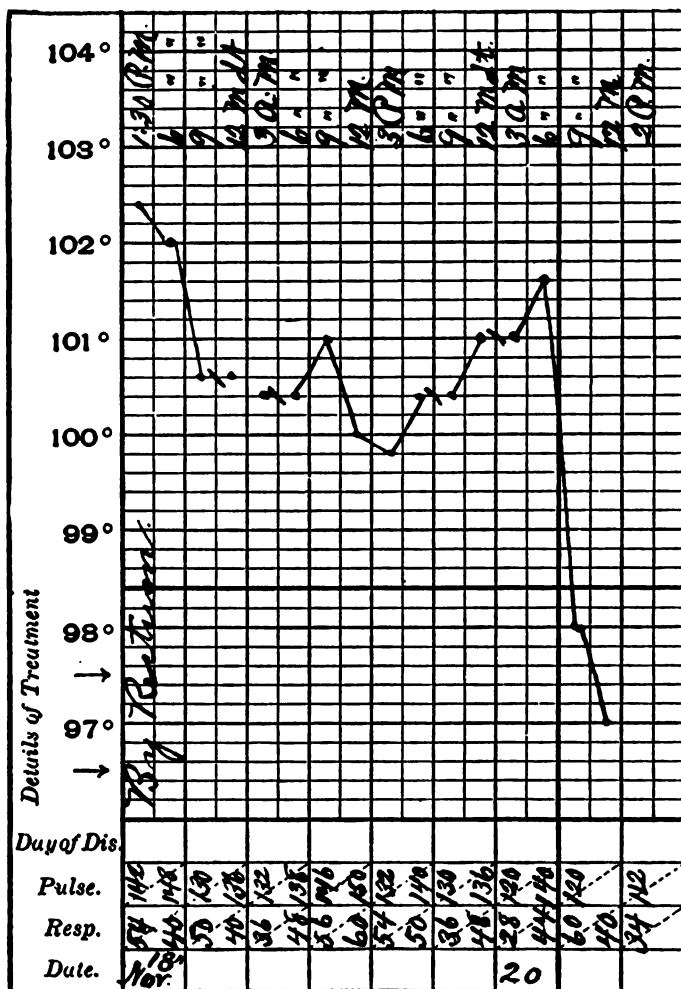
PERSONAL HISTORY.—Child was born naturally, and appeared well up to the sixth month. It then began to have attacks which lasted fifteen to twenty minutes, in which the child would become quite blue all over the body and dyspnea become marked. It would appear weak and depressed for several hours after the attack. These attacks appeared irregularly from two or three daily to one in two weeks. The attacks have persisted since their first appearance. During the week beginning November 10th the child had two attacks of cyanosis, the period of depression lasting much longer than ever before and the child rallying poorly.

On November 17th, an attack of marked cyanosis occurred lasting fifteen to twenty minutes, since which time the child has remained very pale, weak, dyspnea marked and depression very great. The dyspnea has since been a marked feature and at times apparently distressing. The child has an appearance indicative of suffering, the face is drawn, as if from pain. It

* Read before the Philadelphia Pediatric Society, January 14, 1902.

† From the Laboratories of the Jefferson Medical College Hospital.

frets and worries and there is a blue palor about the lips and finger tips. The pupils are dilated and they respond sluggishly to light. They are equal in size. There is no retraction of the



TEMPERATURE CHART.—Case of Congenital Heart Disease.

head or rigidity of the neck. The heart's action is rapid and an occasional irregularity in the pulse is observed. No cardiac murmur is detected. A few râles can be heard over lungs, no change in pulmonary percussion noted.

November 19th.—Examination at 11.45 A.M. Child shows evidences of cyanosis in lips, finger tips, etc. Respiration rapid, 66. Pulse 166. Pupils dilated, respond slowly to light, tongue dry, cries feebly on being moved. No impairment of pulmonary resonance and very few râles in chest, heart sounds rather obscure from rapid respiration, no murmur detected. Knee jerks exaggerated. One attack of cyanosis in last twenty-four hours, blueness well marked for fifteen minutes, slowly fading for several hours; no twitching or convulsive movements noticed since entering hospital. Child can be fed very slowly by dropper taking modified milk mixture $\frac{3}{4}$ i every hour; the eyes are turned upward and to the right, showing very small portions of cornea between half-closed lids. (See chart.)

DIAGNOSIS.—Meningitis non-tubercular. Congenital heart disease.

The autopsy given very fully, by Dr. Rosenberger, showed a beginning meningitis at the convexity; the heart disclosed an interventricular septum deficient at the base, a small opening at the foramen ovale, pulmonary stenosis, and a malposition in the origin of the aorta.

The arrest of development in the case here reported probably occurred between the eighth and twelfth week of fetal life, at this period the septa between the auricles and ventricles have been largely formed and the development of the pulmonary artery and aorta well advanced.

In those cases where a communication exists between the ventricles owing to an imperforate interventricular septum, the opening is usually found at the base, since in fetal life this portion of the septum is formed last. At this portion of the normal heart a triangular area is found, known as the *undefended* space, and this portion of the interventricular wall is more com-

monly found defective in congenital disease than any other portion of the septum. Perforations may occur at the apex or, in fact at any portion of the ventricular septum, but are rare in proportion to the number of openings found in the *undefended* space.

An opening at the base of the interventricular septum may occur as the result of post-natal endocarditis; a few such cases have been reported, notably by M. Bouillard. In this case, however, there can be no doubt as to the congenital origin if the other defects of pulmonary stenosis, patent foramen ovale and origin of aorta be remembered.

The smooth edges of the opening free from any thickening or deposits of fibrin are also typical of congenital disease, although it must be noted that such thickenings and deposits of fibrin are met with following endocarditis in cases of congenital origin.

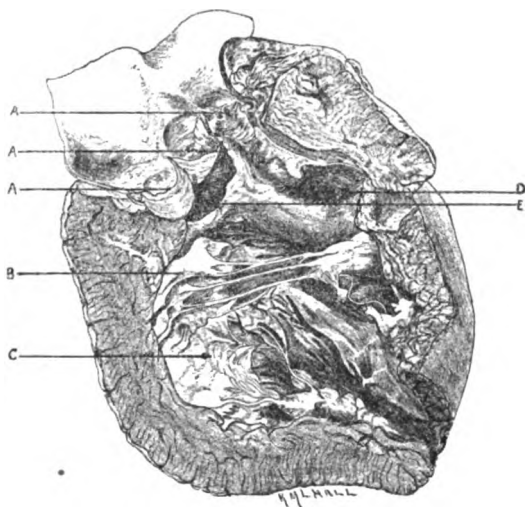
A deviation of the interventricular septum is often found in those cases where the septum is deficient, with consequent change in the position of origin of the pulmonary artery and aorta. Such seems to have been the case in this heart, the aorta arising in part from the right ventricle. This malformation according to Peacock, often coexists with some obstruction to the flow of blood from the right ventricle, as pulmonary stenosis, or more rarely with constriction of one of the auriculo ventricular orifices or of the aortic opening. The presence of pulmonary stenosis in the case presented is therefore explained in the cardiac malformation here described.

PATHOLOGIC REPORT BY DR. R. C. ROSENBERGER.

Body of a well-nourished male infant. Rigor mortis well marked; suggillation is present upon back and buttocks. The panniculus adiposus is abundant; muscles are normal in color.

The abdominal organs are all in normal situation; appendix measures 5 cm. in length and possesses an unusually long mesoappendix.

Both pleuræ are normal. Thymus gland is still evident. It is irregularly ear-shaped and less than 2 cm. in its greatest diameter. It rests upon the superior external surface of the pericardium to which it is adherent.



HEART FROM PATIENT OF DR. GRAHAM.

The right ventricle laid open, incision extending outward through the aorta which communicated with both ventricles. The aorta is open and its valve leaflets are shown at *A A A*.

Between *D* and *E* is the incision which extends outward through the pulmonary artery.

B and *C* are leaflets of the tricuspid valve.

D, the sinus that communicates with the pulmonary artery and constitutes the opening of that vessel into the right ventricle.

E, the semilunar communication between the two ventricles just below the aortic orifice.

Pericardium normal.

The heart presents a depression near the apex 3 mm. in depth. The apex of the organ is blunt and lies in the sixth interspace, $\frac{1}{2}$ inch within mammillary line. Both ventricles

are distended. The organ is shorter than normal, giving it a globular appearance.

The right ventricular wall measures 1.3 cm. in thickness, the left ventricular wall measures 0.7 cm. in thickness. There is a small, crescentic aperture (1.3 cm. by 1 cm.) that forms a communication between the right and left ventricle at the base of the heart. The convexity of the crescent is directed downward and the superior border lies just under the aortic cusps.

The margins of the opening are smooth and thin.

The aorta has its origin from both the right and left ventricle, but principally the right just over the opening already described, and lies above and behind the pulmonary artery. The pulmonary artery arises from the right ventricle, with which cavity it communicates through a small aperture 3 mm. in diameter. It has its origin anterior to the aorta just beneath a muscle column and not recognizable until laid open and traced; the narrow communication with the right ventricle expands at the area of the valves from which point the vessel follows a nearly normal course anterior to the aorta and across the base from right to left. Its branching is normal.

The aorta measures 1 cm. in diameter, the pulmonary artery 5 mm. in diameter. Each of these vessels is supplied with 3 valve leaflets; those of the aorta are normal in thickness while those of the pulmonary artery are thickened and slightly rigid. The mitral valve is normal.

The foramen ovale is closed except for a small slit anteriorly; this opening is oblique, probably closed during life, and admits the passage of a probe 2 mm. in diameter.

The ductus arteriosus (not shown in specimen) is nearly closed, admitting only a small platinum wire. It is normal in point of origin, course and termination. Weight of heart 45 gms.

The left lung is normal. Weight 12 gms.

The right lung is normal except for one small ovoid area of caseation (1 cm. by 0.5 cm.) in upper lobe presenting on the

mediastinal surface. The adjacent lung tissue is normal. Weight of organ 14 gms.

The bronchi show no gross lesion.

The spleen is darker in color than usual, and congested.

Weight 35 gms.

Left adrenal normal.

Apart from very slight congestion the left kidney is normal.

Weight 20 gms.

The right adrenal is normal.

The right kidney is normal. Weight 20 gms.

Ureters are normal.

Bladder is distended with 60 cc. of clear amber-colored urine, walls normal in thickness; mucosa normal.

External genitalia normal.

The liver is slightly smaller than usual and pale. On section it is comparatively bloodless and yellow in color. Weight 430 gms.

Stomach and intestines normal.

Head. The anterior fontanelle measures 8 cm. antero-posteriorly and 4 cm. laterally. The posterior fontanelle is closed. The brain is edematous upon its convexity. Cerebellum is also slightly edematous. No gross lesions.

THE BLOOD CHANGES INDUCED BY THE ADMINISTRATION OF ETHER AS AN ANÆSTHETIC.¹

A CONTRIBUTION FROM THE LABORATORIES OF THE JEFFERSON
MEDICAL COLLEGE HOSPITAL.

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MANY years ago it was asserted that the administration of an anæsthetic has a destructive influence upon the blood. This view was a mere opinion, and was not deduced from well-conceived and carefully performed experiments.

Dr. John Snow believed and taught that an anæsthetic agent suspends the processes of oxidation, and that the essence of the anæsthetic state is suspended oxidation. This view has been advocated in modern times by Richardson, but has of late been entirely overthrown by a recognition of the facts stated by Buxton, that we can produce anæsthesia by hyperoxidation, and that a number of "deoxidizing bodies" are not anæsthetics.

In 1861, Sansom made a report to the Royal Medico-Chirurgical Society, in which he maintained that during anæsthesia quantities of blood-corpuscles are destroyed. He did

¹ Read before the American Surgical Association, May, 1901.

not examine the blood before, during, and after anæsthesia, but made experiments upon blood in test-tubes by adding to it anæsthetic drugs. He found that the addition of an anæsthetic to blood outside of the body destroys the corpuscles and liberates coloring matter. The above method was, of course, inconclusive, could give no positive information, and was, at most, merely suggestive.

In 1869, Dr. J. H. McQuillen (*Dental Cosmos*, March, 1869) made a series of experiments in order to determine the condition of the corpuscles of the blood during the anæsthetic state. He examined the blood of a number of human beings prior to and after the administration of ether, chloroform, and nitrous oxide, and stated that he found no evidence of corpuscular destruction.

In 1890, Mikulicz (*Beilage zum Centralblatt für Chirurgie*, 1890, No. 25) presented the studies of a pupil, Bierfreund, in regard to the amount of hæmoglobin in the blood in surgical diseases, with especial reference to its restoration after the occurrence of hæmorrhage. He mentioned in this paper that the administration of chloroform may reduce the hæmoglobin from 5 to 10 per cent.

In 1893, Garrett and Oliver (*Lancet*, September 9, 1893), as a result of numerous experiments, arrived at the conclusion that anæsthetics, particularly chloroform, deoxidize the blood and also the tissues, and thus induce malnutrition and the formation of quantities of waste products, the elimination of these toxic products causing a severe, and possibly a dangerous or even a fatal, strain upon the excretory glands. Garrett and Oliver also pointed out the fact that a patient under the influence of ether sweats profusely, a process which lowers the temperature, the temperature being also lowered by the evaporation of ether and by depression of the nervous system. In this paper we point out that the sweating which occurs under ether must be taken into consideration in estimating blood changes.

In 1895, one of us (J. Chalmers Da Costa) made an investigation of the action of ether upon the blood, he being at

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that time unaware of Mikulicz's observations upon chloroform, or of any other studies of a like sort. The experiments were published in the *Medical News* of March 2, 1895. The blood was examined before, during, and after etherization. Twenty-seven cases were studied; in the majority there was a distinct fall in hæmoglobin. It was also observed that the red corpuscles were often altered in shape, but that they were not diminished in number. The diminution in the amount of hæmoglobin was found to be most marked in anæmic individuals,—an observation which seems to afford an explanation of the reason why operative shock is usually so profound and prolonged in the anæmic. In Da Costa's cases the counts were made by means of a Thoma-Zeiss hæmocytometer, and the hæmoglobin was estimated by the instruments of Gowers and Fleischl. That the fall in hæmoglobin was not entirely due to the hæmorrhage was indicated by the fact that it occurred in some bloodless cases; for instance, an examination of a strictured rectum, the reduction by taxis of an inguinal hernia, and the breaking up of adhesions in an ankylosed metacarpophalangeal joint. It was also noted that ether given as an anæsthetic markedly lowers the temperature. This fall of temperature begins with the anodyne stage, and averages from 1° to 3° F., but may reach 4° or even 5° F. That the fall is not due purely to shock is proved by its occurrence in trivial operations, and by the rapid ascent of the temperature on suspending the administration of the anæsthetic.

Among the conclusions deduced from these experiments are the following:

“Etherization produces a marked diminution in the hæmoglobin of the blood.

“The red corpuscles and the hæmoglobin are especially affected in blood previously diseased.

“Irregular records are due to faulty observation; to the presence of altered hæmoglobin in the blood; to the faulty aberration as to color of a Fleischl instrument or to taking blood before anæsthesia is complete.

“The white corpuscles show irregular changes which are

not characteristic, and exhibit variations not more pronounced than would be found in the same number of samples of normal blood on different examinations.

“ Age does not apparently influence the results.

“ The often-quoted observation as to the effect upon the hæmoglobin of shock and hæmorrhage requires enlarged repetition of the experiments upon human beings, before the statements that hæmorrhage causes a great fall in the amount of hæmoglobin, but that shock does not affect it, can be accepted.

“ Prolonged anæsthesia profoundly deteriorates the blood and strongly militates against recovery; hence, rapidity of operation is most desirable.”

One or two other conclusions which do not seem to bear upon our present study are not cited.

The above-quoted studies, if correct, indicate that the blood of a patient should be examined before an anæsthetic is administered; and that if marked anæmia exists, or if the amount of hæmoglobin is lowered, the administration of an anæsthetic must be regarded with apprehension. If it is found necessary to employ one, it must be administered by a skilled anæsthetist. As little as possible should be given; oxygen should be administered with it; the surgeon should work rapidly; the patient should be carefully protected from cold, and vigorous efforts to bring about reaction should be promptly made as soon as the operation is complete, or even during its performance. If the amount of hæmoglobin is very low, no general anæsthetic should be given.

Da Costa made no attempt to obtain information as to the lowest amount of hæmoglobin which is consistent with the fairly safe administration of an anæsthetic. Mikulicz estimates it at 30 per cent. for chloroform. He believes that the administration of chloroform when the hæmoglobin is only 20 per cent. will be followed by respiratory paralysis. In three patients that died of operative collapse, Mikulicz found but 15 per cent. of hæmoglobin remaining in the blood.

These views in regard to the deteriorative influence of ether upon the blood have been accepted by some and re-

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jected by others. It has been generally accepted that ether causes leucocytosis, which is probably of a toxic character; but its action upon the red corpuscles and hæmoglobin is still a matter of dispute. Von Lerber (*Centralblatt für Gynäkologie*, No. 19, 1897) reports a study of the blood in 101 cases after the inhalation of ether. He asserts that in most instances the hæmoglobin was unaltered. He found leucocytosis, but the red corpuscles were very little changed, either in number or in appearance. He made a spectroscopic study of the urine; but as he was unable to find urobilin, he concludes that ether does not exert any harmful influence upon the blood, and does not set free hæmoglobin. The belief that because urobilin is not discovered in the urine, none is set free in the blood, is, to our mind, not warranted by conclusive observations. Von Lerber points out that the more prolonged the anæsthesia the more marked is the leucocytosis.

Oliver (*Lancet*, June 27, 1896) says that observations should be made upon animals, in order to determine whether normal red corpuscles are affected by ether. He believes that observations made before, during, and after operations are entirely unreliable, because the operation, whether or not it is accompanied by bleeding, disturbs the composition of the blood. Oliver made a number of observations upon rabbits, keeping each animal under the influence of the anæsthetic for one hour. He found the average blood decimal to be 1.1 before anæsthesia and .98 after anæsthesia; during anæsthesia the corpuscles appeared to be normal, and there were apparently no injurious after-effects. He says that this indicates that ether does not affect normal red corpuscles, but admits that it may affect those that are diseased; and he is quite sure that the resisting power of the stroma of the corpuscles must vary under the influence of ether.

Dudley W. Buxton (*Lancet*, February 1, 1896) says: "In every case, blood removed from the body and shaken with an anæsthetic shows destruction of the corpuscles and reduction with pouring out of hæmoglobin; and it would also appear that a similar, if less marked, phenomenon occurs in the body." Through some observations which he has made, Buxton has become persuaded that there is a decided diminution in hæmo-

globin when an animal is under the influence of ether, chloroform, or nitrous oxide. He says: "It is, however, not improbable that factors other than the anæsthetics may be found at work in bringing about this result. The combination or association between the gaseous anæsthetics or vapors and the constituents of the blood must be a loose one, since in their presence oxygen is displaced. Were they to form combinations as stable as that which carbonic oxide establishes, not only would the anæsthetic displace the oxygen, but it would render impossible the re-formation of oxyhæmoglobin; hence, death must result." Buxton goes on to state that it is impossible to say whether the corpuscles, in some cases after the administration of an anæsthetic, have a lessened power of taking up oxygen; but that it seems probable that such is the case.

Hamilton Fish (*ANNALS OF SURGERY*, July, 1899) has contributed an extremely valuable article, which he designates, "The Importance of Blood Examinations in Reference to General Anæsthetization and Operative Procedures." He takes the affirmative on the question of whether or not ether reduces hæmoglobin and affects red corpuscles. He believes that anæsthesia may lessen tissue resistance, and thus lead to septic lesions; and he thinks that the condition of the blood is a fairly accurate gauge of the patient's general condition, and that the blood should always be examined before the administration of an anæsthetic. He says that those that labor under neurasthenia, anæmia, chlorosis, leukæmia, and the lymphatic temperament have blood in which marked changes can be demonstrated; and that all of these patients stand operations, and also anæsthesia, badly. Fish advocates the view that an anæsthetic extracts oxygen from oxyhæmoglobin, and combines with the latter; and he further asserts that in patients with less than 50 per cent. of hæmoglobin, oxygen is taken away from corpuscles which are so poor in that element that they cannot spare it. As a consequence, such corpuscles are unable to give up any oxygen to the tissues; and these patients, when under the influence of ether, will show evidences of collapse. Fish reminds us that respiration depends upon the nervous system and upon the amount of hæmoglobin in the blood, and that if hæmoglobin is reduced below a certain limit respiration ceases. He thinks that the minimum is 20 per cent., and refers to the observation of Mikulicz that

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in three cases dying of collapse during operation 15 per cent. of hæmoglobin was found remaining in the blood. In Fish's opinion, the safest rule is not to give an anæsthetic if the hæmoglobin is under 50 per cent.; anything above 80 per cent. he considers normal. An amount of anæsthetic which is perfectly harmless when there is 80 per cent. of hæmoglobin may be extremely dangerous when there is but 50 per cent. Fish also points out the important fact that safe anæsthesia depends not alone upon a good percentage of hæmoglobin, but also upon the existence of a normal or increased number of polynuclear neutrophiles. He regards the leucocytosis of anæsthesia as phagocytic in character, and as a measure of individual resistance. He believes that the blood should be examined not only before but during anæsthesia; because the first evidence of approaching danger may be found in a blood change. He also points out the interesting fact that at an altitude of one mile normal hæmoglobin is reduced from 12 to 15 per cent. during the first hour of anæsthesia.

Dr. Joseph G. Bloodgood, of the Johns Hopkins Hospital ("Progressive Medicine," Vol. iv, 1900), in reviewing Dr. Hamilton Fish's article, entirely agrees with that author's conclusions, and cites several cases occurring in the Johns Hopkins Hospital to confirm these views.

From the above quoted opinions it will be observed that wide divergences exist among the views of the different writers upon this subject,—between the views which J. Chalmers Da Costa put forth in 1895 and the results of the experiments upon rabbits made by Oliver; between the broad affirmation of the belief that ether lowers hæmoglobin and has a destructive influence upon corpuscles, in the article by Hamilton Fish, the absolute denial of this by Von Lerber, and the rather conservative opinion of Dudley Buxton. The controversialists are like the two knights of allegory who stood upon opposite sides of the shield, disputing as to the words graven upon it; each one saw his own side, and each was right and both were wrong. It becomes evident that some of the observations must be entirely erroneous; or else undiscovered factors and unrecognized elements exist in the problem, which make all previous observations never entirely correct and never

completely wrong. These discrepancies and disagreements may depend upon the personal equation; upon the employment of different methods to estimate the hæmoglobin; upon the different altitudes above the sea at which the experiments were made; upon the daily and nightly oscillations which are known to occur in the percentage of hæmoglobin and corpuscles; upon the uncertain results obtained by the hæmoglobinometer; upon the different methods taken to secure the blood, and the fact that it may have been taken from different portions of the body; upon the fact that the extremity from which the blood was taken may or may not have been elevated, and also that massage and manipulation may or may not have been employed; upon the fact that in some cases digestion may have been going on, while in others it may not have been; and particularly upon the fact that in some cases the blood may have been concentrated by purgation and diaphoresis, while in others it may not have been.

In Da Costa's former cases the patients were in many instances taken from the dispensary and etherized without previous preparation. In this new series of cases we determined that the patients should be those carefully prepared for operation,—a preparation which involves concentration of the blood by purgation, which concentration is usually added to by profuse sweating during the anæsthetic state. We further determined to have all the blood examinations made by a thoroughly competent third party, who would make them all in exactly the same manner, who would have no view of his own, and who would not be lured from the path of accurate observation by any theoretical Jack-a-lantern. We selected for this work Dr. A. G. Ellis, the Pathological Resident of the Jefferson College Hospital, who performed it with the utmost skill and care; and we wish here to extend to him our thanks. Further, we decided that the table, when completed, should be broken up into numerous sub-tables, according to the time before and after operation when the blood was examined; to the duration of the anæsthesia; to the amount of ether used; to the estimated quantity of blood lost, etc. It is our aim in these investigations to consider the sub-

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ject, as far as possible, from a practical rather than from an experimental stand-point. We concluded to gather fifty cases, taken out of the general run of patients in a busy hospital,—the Jefferson Medical College Hospital. The cases were selected from the various wards,—surgical, gynæcological, etc. The blood examinations, which were made before and after the operations, consisted of the estimation of the number of erythrocytes, the hæmoglobin percentage, the color index, and the number of leucocytes. Differential counts of the leucocytes were not undertaken, for it was not our object to study the leucocytic changes in detail. The results of the blood examination before the operation were compared with those after the operation. It was practically impossible to always set a definite time before the operation, as the period in which the observation should be made, so we decided to make the examination in a number of cases within a reasonable period preceding operation; that is, within some hours of the time of going to the operating room. In other instances the blood examinations were made some time before going to the clinic room, on account of postponement of the operation. In some cases examination was deliberately made a considerable time before operation, in order to anticipate preparatory methods of treatment. Similar difficulties were encountered in arriving at the proper time for the blood examinations after the operation. The counts following the operation were made either immediately after or upon the day following. Examinations were not made during the anæsthetic state; for our particular aim was to determine the changes which follow etherization, rather than the changes that are evident during the anæsthetic period.

Blood Concentration.—The problem of blood concentration naturally presented itself, for the preparatory operative treatment includes measures which tend to increase the elimination of the watery principles of the body, while the intake of fluids is always reduced prior to and for a time after the operation. The general rules governing preparatory measures of treatment at the Jefferson Medical College Hospital consist in

- (a) A hot bath;
- (b) Active purgation;
- (c) Reduction of diet, and withholding of all food and liquid for some hours preceding the operation;
- (d) Occasionally the administration of heart stimulants.

Cause of Blood Concentration.—It is generally admitted that such conditions as increased blood pressure, diarrhoea, profuse sweating, frequent vomiting, and the withdrawal of a large quantity of serous fluid,—which is rapidly replaced by the transfusible elements of the blood,—and deprivation of fluids, all tend to produce blood inspissation. It is a well-known fact that the blood of individuals suffering from Asiatic cholera shows concentration to a high degree. The finding of 6,000,000 or more red blood-cells per cubic millimetre in this disease is not unusual. Cabot ("Clinical Examination of the Blood"), in referring to the work of Hay, "On the Action of Saline Cathartics," states that "Hay gives the following figures, showing the effect of sulphate of sodium in concentrating the blood: Subject, a healthy man of thirty-three years of age. 3.35 P.M., red corpuscles, 5,250,000; was given 85 cubic centimetres of a concentrated solution of sulphate of sodium in water. Thirty-five minutes later, the blood count showed red corpuscles, 6,540,000; sixty-five minutes later, it showed red corpuscles, 6,790,000; and four hours later, red corpuscles, 4,930,000. Evidently much fluid was drawn out of the blood-vessels; and then within four hours the tissues had supplied the loss, and the blood had returned to its normal density. Hay also showed that a dilute solution of the same drug had far less effect in concentrating the blood. Further, he demonstrated that if blood is already concentrated when the saline is given, no purgative effect follows."

Concentration is well shown after profuse sweating. Oliver (*Lancet*, June 27, 1896) reports temporary apoplasia produced by a Turkish bath. In this case the corpuscular percentage was 91 before the bath, while immediately after the bath it was 106, and two hours after the bath the percentage fell to almost 99. Thirty ounces of beer were ingested half an hour after the bath.

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Oliver, in referring to the variations in the volume of the plasma, states that "when, for example, the output of water, whether by the kidneys, the skin, or the bowels, temporarily exceeds the income, the volume of the plasma is for a time reduced, and there is a proportionate rise in the corpuscles." He further states that "the concurrent variations in the percentage of the corpuscles and hæmoglobin, which have been so repeatedly pointed out, are indeed volumetric indications of the circulation of the water into or from the blood; into it from the digestive tract and the tissues, and from it by the kidneys, skin, and lungs, and probably into the muscles during exercise. The blood is continually tending to balance its income and output of water, and is thus always striving for a mean; but, notwithstanding this wonderful, persistent adjustment, variations in the proportion of water present in the plasma are, at the same time, shown by these observations to be constantly taking place within certain physiological limits." Blood inspissation is also produced by increased blood pressure; for example, small doses of suprarenal extract increase arterial tension, thereby favoring the elimination of water, and consequently inducing polycythæmia. It is worthy of mention that in the blood concentration occurring in the healthy individual, within the physiological limits, the rise in the corpuscular and hæmoglobin percentage is parallel; the blood decimal, therefore, does not change. The rapidity with which the blood loses some of its diffusible elements, therefore, must always be borne in mind; and the rapidity with which the blood again dilutes is a matter no less important. It is undoubtedly true that the loss of the watery elements of the plasma is only transitory; nevertheless, the rapidity with which the blood tends to reach the normal probably varies greatly in individual cases, and is modified by many factors. The following statement of Cabot ("Clinical Examination of the Blood"), in regard to the subject of blood concentration, is indeed worthy of careful consideration at all times, when dealing with blood examinations. "In the presence, therefore, of any such reason for

the concentration of the blood, we should always modify our ordinary methods of inference from the blood counts."

Blood Destruction (Hæmolysis) and Blood Formation (Hæmogenesis).—In health, the number of erythrocytes and the amount of hæmoglobin maintain a uniform standard; the formation of the new red blood-cells and the destruction of the colored elements progresses uniformly. The subject of the average life of the erythrocytes has received much discussion, but still remains an unsettled question. It has been suggested that the average duration of the life of the chromocyte appears to be about two weeks or less; therefore 357,152 red blood-cells per cubic millimetre are destroyed each day. In other words, the destruction is at the rate of 248 per minute in each cubic millimetre of blood. Hæmogenesis progresses accordingly.

Blood Regeneration.—In order to base our conclusions upon scientific principles, it is essential to consider the generally accepted views governing blood regeneration. These may be summarized as follows: Immediately following the loss of blood (for example, in a traumatic hæmorrhage), the erythrocytes and the hæmoglobin are reduced proportionately; in a short time the other tissues of the body compensate for the volume of fluid lost from the blood. Following this dilution, erythrocytic regeneration progresses rapidly, and the number of corpuscles lost is restored to the proper level in a short time; the hæmoglobin, however, is not replaced so quickly. Therefore, the newly formed corpuscles in the circulation are deficient in coloring matter, and the total hæmoglobin percentage is below the corpuscular percentage; consequently, there is a reduction in the average blood decimal. After the lapse of some time the hæmoglobin is restored, and the erythrocytic regenerative properties of the blood-making organs gradually become normal.

Blood Concentration and Anæmia.—Blood concentration may progress or be associated with anæmic states. In cases of this kind the total volume of the blood is reduced; the number of erythrocytes may appear to be normal or to exceed the normal; while the hæmoglobin will not present the same

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increase, although the percentage may be increased; but the total amount is diminished, as is shown by the lowered color index. When the blood becomes diluted and inspissation disappears, the percentage of corpuscles and hæmoglobin is lowered; while the blood decimal remains unaltered unless improvement follows, which will be indicated by a rise in the corpuscular hæmoglobin value.

RECORDS.

In gathering our clinical data, we particularly emphasize the points bearing upon the conditions which produce blood inspissation, endeavoring to determine, therefore, in a general way the loss of the watery constituents of the body. The task of gathering the clinical notes was assigned to the Resident Physicians of the Jefferson College Hospital. The following chart was prepared so as to facilitate their work:

Number.... Name..... Age..... Sex..... Date.....
Nativity..... Occupation..... Ward..... Doctor.....
Diagnosis..... Date of Admission.....
Date of Discharge.....
Revised Diagnosis..... Result.....
.....
History
Physical Examination.....
Character and Amount of Urine in Twenty-four Hours before and after
Anæsthesia
Character and Amount of Vomit before and after Anæsthesia.....
Character and Amount of Bowel Movement before and after Anæsthesia
Amount of Sweating before and after Anæsthesia.....
Remarks. (Was any large quantity of fluid lost before or after operation?)
Date, Hour, and Character of Operation.....
Blood Loss.....
Duration of Anæsthesia.....
Character and Amount of Anæsthetic.....

Blood Examination.

Date and Hour before Operation.	Date and Hour after Operation.
Hæmoglobin	Hæmoglobin
Erythrocytes	Erythrocytes
Leucocytes	Leucocytes
Color Index.....	Color Index.....

Hæmatological Examination.—In procuring the blood for examination, the following rules were always observed: The

patients were in the recumbent posture. The blood was taken from the tip of the finger. In no case was the hand œdematous. The skin was cleaned with water or a little soap and water; next, with alcohol, and was then dried. The part was warmed by a gentle friction; care was taken not to excite hyperæmia by a vigorous rubbing. The puncture was effected with a clean needle having a cutting surface, and was made deep enough to insure a free flow of blood with out squeezing the part near the wound. The first drop was always wiped away. The number of erythrocytes and leucocytes was estimated with the Thoma-Zeiss hæmocytometer. In determining the number of the red cells, a 2 per cent. salt solution was used as a diluent, in the proportion of one part of blood to 200 parts of the solution. A 1 per cent. acetic acid solution was used as the diluting fluid, in the proportion of 1 to 20, in estimating the number of leucocytes. In ascertaining the number of erythrocytes, the corpuscles over eighty squares were counted; while the corpuscles over 400 squares were enumerated in determining the number of leucocytes. The hæmoglobin estimations were made with Oliver's hæmoglobinometer, except in four cases in which the Fleischl instrument was employed.

Tabulation of Cases.—After the various facts had been collected, the fifty cases were arranged in a tabular form. The facts included in this table are the name, sex, nativity, and occupation of the patient; the ward, the diagnosis, the date of admission, the date of discharge, the result, the character of the operation, the date and hour of the operation, the estimated blood loss, the anæsthetic employed, the amount of the anæsthetic used, the duration of the period of anæsthesia, the date and hour of the blood examination before the operation (the examination includes the hæmoglobin percentage, the number of erythrocytes per cubic millimetre, the number of leucocytes per cubic millimetre, and the color index), the date and hour of the blood examination after the operation, which again includes the hæmoglobin percentage, the number of erythrocytes per cubic millimetre, the number of leucocytes per cubic millimetre, and the color index.

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TABLE I.

Case No.	BEFORE ANÆSTHESIA.			AFTER ANÆSTHESIA.			DIFFERENCE.		
	Corpuscles.	Color Index.	Hæmo. per cent.	Corpuscles.	Color Index.	Hæmo. per cent.	Cor. Loss or Gain.	Hæmo. Loss or Gain.	Color Index Loss.
1.	3,245,000	.89	58	3,920,000	.76	60	675,000+	2+	.13
2.	4,170,000	.9	75	5,390,000	.742	80	1,220,000+	5+	.158
3.	3,795,000	.724	55	4,330,000	.577	50	535,000+	5—	.147
4.	4,050,000	.92	75	5,160,000	.82	85	1,110,000+	10+	.10
5.	5,340,000	.889	95	5,370,000	.884	95	30,000+	0+0—	.005
6.	5,130,000	.926	95	5,250,000	.9	95	120,000+	0+0—	.026
7.	4,575,000	.82	75	4,600,000	.76	70	25,000+	5—	.06
8.	4,680,000	.908	85	4,850,000	.824	80	170,000+	5—	.084
9.	4,750,000	.863	82	4,620,000	.811	75	130,000—	7—	.052
10.	4,520,000	.94	85	4,950,000	.808	80	430,000+	5—	.132
11.	4,500,000	.944	85	4,240,000	.943	80	260,000—	5—	.001
12.	4,375,000	.857	75	4,387,000	.683	60	12,500+	15—	.174
13.	3,820,000	.982	75	4,810,000	.779	75	990,000+	0+0—	.203
14.	5,660,000	.75	85	5,490,000	.728	80	170,000—	5—	.022
15.	5,210,000	.959	100	5,360,000	.886	92	150,000+	5—	.073
16.	3,680,000	.87	64	5,230,000	.592	62	1,550,000+	2—	.278
17.	4,160,000	.841	70	3,900,000	.77	60	260,000—	10—	.071
18.	4,940,000	.88	87	5,600,000	.848	95	660,000+	8+	.032
19.	5,140,000	.826	85	4,850,000	.824	80	290,000—	5—	.002
20.	4,710,000	.934	88	5,925,000	.798	95	1,215,000+	7+	.136
21.	5,560,000	.809	90	5,800,000	.801	93	240,000+	3+	.008
22.	5,190,000	.915	95	5,880,000	.85	100	690,000+	5+	.065
23.	4,920,000	.945	93	5,740,000	.827	95	820,000+	2+	.118
24.	3,970,000	1.000	80	3,890,000	.964	75	80,000—	5—	.036
25.	4,440,000	.822	73	5,650,000	.796	90	1,210,000+	17+	.026
26.	4,780,000	.868	83	4,870,000	.739	72	90,000+	11—	.129
27.	4,820,000	.964	83	5,137,000	.924	95	317,000+	12—	.040
28.	5,430,000	.874	95	6,130,000	.792	100	700,000+	5+	.082
29.	5,650,000	.911	103	6,070,000	.807	98	420,000+	5—	.104
30.	5,070,000	.936	95	6,375,000	.902	115	1,305,000+	20+	.034
31.	4,880,000	.922	90	5,360,000	.904	97	480,000+	7+	.018
32.	5,480,000	.865	95	6,620,000	.83	110	1,140,000+	15+	.035
33.	5,520,000	.995	110	6,120,000	.776	95	600,000+	15—	.219
34.	5,160,000	.92	95	6,000,000	.862	105	930,000+	10+	.058
35.	5,040,000	.992	100	5,720,000	.83	95	680,000+	5—	.162
36.	5,590,000	.983	110	6,225,000	.963	120	635,000+	10+	.020
37.	5,890,000	.933	110	6,710,000	.842	113	820,000+	3+	.091
38.	6,130,000	.938	115	5,380,000	.93	100	750,000—	15—	.008
39.	3,900,000	.641	50	4,060,000	.492	40	160,000+	10—	.149
40.	6,280,000	.954	120	6,070,000	.93	113	210,000—	7—	.024
41.	6,100,000	.983	120	6,170,000	.988	122	70,000+	2+	+
42.	4,920,000	.873	80	5,300,000	.66	70	380,000+	10—	.213
43.	5,550,000	1.030	115	6,030,000	.829	100	480,000+	15—	.201
44.	4,600,000	1.000	92	5,050,000	.891	90	450,000+	2—	.109
45.	5,350,000	.981	105	4,880,000	.922	90	470,000—	15—	.059
46.	4,880,000	1.020	100	6,040,000	.91	110	1,160,000+	10+	.11
47.	5,330,000	.863	92	5,750,000	.782	90	420,000+	2—	.081
48.	4,700,000	.957	90	5,120,000	.859	88	420,000+	2—	.098
49.	5,500,000	.936	103	5,700,000	.831	95	200,000+	8—	.105
50.	5,940,000	.942	112	6,080,000	.904	110	140,000+	2—	.038
Aver.	4,977,440	.903	89	5,126,800	.821	86+	149,360+	3—	.082

GENERAL SUMMARY OF THE BLOOD CHANGES.

Erythrocytes.—The number of chromocytes was increased in forty-one cases and decreased in nine. The average count before the operation was 4,977,440; the average count after the operation was 5,126,800; and the gain was 143,360 per cubic millimetre.

Hæmoglobin.—The average hæmoglobin percentage preceding the anæsthetic state was 89; the average hæmoglobin percentage following the anæsthetic state was 86, showing a loss of 3 per cent. The hæmoglobin revealed an apparent increase in nineteen cases, and a decrease in twenty-eight cases, and there was no loss or gain in three instances. The average gain in the nineteen cases was 8.05 per cent., while the average loss in the twenty-eight cases was 7.25 per cent.

Color Index.—The average individual corpuscular hæmoglobin value preceding the operation was .903, while that following was .821, showing an average loss of .082. In forty-nine out of the fifty cases, the blood decimal was reduced after the operation. In one instance only was the color index slightly increased after the anæsthetic state. This occurred in Case No. 41. The color index preceding the operation was .983, and that following the operation was .988; in this instance the blood decimal was practically unchanged.

Leucocytes.—The number of leucocytes varied greatly before and after the operation. The average count preceding the operation was 9898, and the average count following was 14,484, showing an average gain of 4586 per cubic millimetre. In forty-three instances the leucocytes were increased, while in nine instances the number was decreased after the operation.

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TABLE II.

Group A.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Time between Blood-Count before Operation and Operation.		Time between Operation and Blood-Count after Operation.	
6.	3	hours and 15 minutes.	6	hours.
7.	2	"	5	"
8.	3	"	5	"
9.	2	"	4	"
10.	2	"	4	"
13.	1	"	2	"
18.	3	"	5	"
29.	3	"	6	"
36.	2	"	4	"
37.	1	"	5	"
40.	2	"	6	"
41.	1	"	3	"
44.	2	"	4	"
45.	1	"	4	"
49.	3	"	4	"
Average	2	"	4	"

Group B.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOME TIME AFTER ANÆSTHESIA.

Number.	Time between Blood-Count before Operation and Operation.		Time between Operation and Blood-Count after Operation.	
11.	2	hours and 45 minutes.	17	hours and 30 minutes.
12.	1	"	21	"
14.	2	"	22	"
19.	1	"	21	"
22.	2	"	21	"
23.	2	"	20	"
25.	5	"	22	"
26.	1	"	24	"
27.	4	"	21	"
28.	3	"	17	"
30.	4	"	19	"
32.	3	"	19	"
33.	2	"	21	"
34.	1	"	22	"
35.	3	"	19	"
38.	3	"	21	"
42.	3	"	21	"
43.	3	"	21	"
46.		"	23	"
47.	3	"	20	"
48.	2	"	22	"
50.	2	"	22	"
Average	2	"	20	"

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Group C.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Time between Blood-Count before Operation and Operation.	Time between Operation and Blood-Count after Operation.
5.	19 hours and 55 minutes.	4 hours and 5 minutes.
16.	23 "	1 "
21.	16 "	7 " 45 "
Average	19 " 38 "	4 " 16 "

Group D.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOME TIME AFTER ANÆSTHESIA.

Number.	Time between Blood-Count before Operation and Operation.	Time between Operation and Blood-Count after Operation.
1.	23 hours and 10 minutes.	19 hours and 5 minutes.
2.	29 " 23 "	19 " 7 "
3.	25 " 10 "	20 " 50 "
4.	69 " 30 "	18 "
15.	72 "	19 "
17.	23 "	21 " 30 "
20.	24 " 30 "	22 " 30 "
24.	19 " 30 "	19 " 30 "
31.	98 " 30 "	21 "
39.	26 "	20 "
Average	41 " 1 "	20 " 3 "

CLASSIFICATION OF CASES.

So as to carefully compare the blood disturbances, it was found necessary to group the cases into four classes. This was done in order to find what bearing the preparatory and postoperative measures associated with the anæsthetic period have upon the blood disturbances. (See Table II.) In Group A those cases are included in which the first blood examination was made a short time before anæsthesia (average, 2 hours and 21 minutes), and soon after anæsthesia (average, 4 hours and 41 minutes). The cases included in Group B are those in which the blood examinations were made a short time before the operation (average, 2 hours and 51 minutes), and some time afterwards (average, 20 hours and 59 minutes). The cases in Group C include those in which the blood examination was made some time preceding the operation (average, 19 hours and 38 minutes) and soon after (average, 4 hours and 16 minutes). The cases included in

BLOOD CHANGES INDUCED BY ETHER.

Group D are those in which the blood examination¹ was made a considerable time before (average, 41 hours and 1 minute) and some time after the operation (average, 20 hours and 3 minutes).

In Group A, the result of the examination represents the changes that immediately follow the anæsthetic state; the first blood count, however, being made after the preparatory measures of treatment had been instituted, and the second count before the postoperative treatment had been fairly begun. In Group B, the results show, in a general way, the effects of the anæsthetic state and the postoperative treatment. The count preceding the operation was, however, made during or at the height of the preparatory treatment. In Group C the results represent the blood changes which occur during the preparatory treatment and during the anæsthetic state. In Group D the results include the effects produced by the preparatory treatment, the anæsthetic state, and the postoperative measures. Fifteen cases are included in Group A, 22 in Group B, 3 in Group C, and 10 in Group D.

TABLE III.

Group A.

Num- ber.	First Count, made just before Anæsthesia.	Second Count, made just after Anæsthesia.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
6.	5,130,000	5,250,000	120,000		.026
7.	4,575,000	4,600,000	25,000		.06
8.	4,680,000	4,850,000	170,000		.084
9.	4,750,000	4,620,000		130,000	.052
10.	4,520,000	4,950,000	430,000		.132
13.	3,820,000	4,810,000	990,000		.203
18.	4,940,000	5,600,000	660,000		.032
29.	5,650,000	6,070,000	420,000		.104
36.	5,590,000	6,225,000	635,000		.02
37.	5,890,000	6,710,000	820,000		.091
40.	6,280,000	6,070,000		210,000	.024
41.	6,100,000	6,170,000	70,000		+slight.
44.	4,600,000	5,050,000	450,000		.09
45.	5,350,000	4,880,000		470,000	.059
49.	5,500,000	5,700,000	200,000		.105
Average			265,000		.077

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Group B.

Num- ber.	First Count, made just before Anæsthesia.	Second Count, some time after Anæsthesia.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
11.	4,500,000	4,240,000		260,000	.001
12.	4,375,000	4,387,500	12,500		.174
14.	5,660,000	5,490,000		170,000	.022
19.	5,140,000	4,850,000		290,000	.002
22.	5,190,000	5,880,000	690,000		.065
23.	4,920,000	5,740,000	820,000		.118
25.	4,440,000	5,650,000	1,210,000		.026
26.	4,780,000	4,870,000	90,000		.129
27.	4,820,000	5,137,000	317,000		.040
28.	5,430,000	6,130,000	700,000		.082
30.	5,070,000	6,375,000	1,305,000		.034
32.	5,480,000	6,620,000	1,140,000		.035
33.	5,520,000	6,120,000	600,000		.219
34.	5,160,000	6,090,000	930,000		.058
35.	5,040,000	5,720,000	680,000		.162
38.	6,130,000	5,380,000		750,000	.008
42.	4,920,000	5,300,000	380,000		.213
43.	5,550,000	6,030,000	480,000		.201
46.	4,880,000	6,040,000	1,160,000		.11
47.	5,330,000	5,750,000	420,000		.081
48.	4,700,000	5,120,000	420,000		.098
50.	5,940,000	6,080,000	140,000		.038
Average			460,204		.084

Group C.

Num- ber.	First Count, some time before Anæsthesia.	Second Count, some time after Anæsthesia.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
5.	5,340,000	5,370,000	30,000		.005
16.	3,680,000	5,230,000	1,550,000		.278
21.	5,560,000	5,800,000	240,000		.008
Average			740,000		.097

Group D.

Num- ber.	First Count, some time before Anæsthesia.	Second Count, made just after Anæsthesia.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
1.	3,245,000	3,920,000	675,000		.13
2.	4,170,000	5,390,000	1,220,000		.158
3.	3,795,000	4,330,000	535,000		.147
4.	4,050,000	5,160,000	1,110,000		.10
15.	5,210,000	5,360,000	150,000		.073
17.	4,160,000	3,900,000		260,000	.071
20.	4,710,000	5,925,000	1,215,000		.136
24.	3,970,000	3,890,000		80,000	.036
31.	4,880,000	5,360,000	480,000		.018
39.	3,900,000	4,060,000	160,000		.149
Average			520,000		.102

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Number of Erythrocytes.—The average gain per cubic millimetre in Group A was 265,000; twelve cases in this class showed a gain in the number of colored corpuscles, while there was a loss in three cases. (See Table III.)

The average gain per cubic millimetre in Group B was 460,204 corpuscles; and there was an increase in the number of erythrocytes in eighteen cases and a decrease in four cases.

The average gain per cubic millimetre in Group C was 740,000 corpuscles; every case in this group showed an increase in the number of red cells.

In Group D the average gain was 520,000 corpuscles per cubic millimetre; eight cases showed an increase in the number of chromocytes, and two cases showed a decrease.

In Series A, Cases 9, 40, and 45, and in Series B, Cases 11, 14, 19, and 38, indicate that the preparatory treatment produced marked concentration of the blood, which was probably at its height at the time of the first examination or a short while afterwards, the blood having become somewhat diluted before the second count was made. In the remaining cases of Series A and B, the marked increase in the number of erythrocytes must be attributed to the blood inspissation. In Series C, a gain in the number of chromocytes only was noted. This was probably due to the fact that two of the factors which produce blood inspissation, namely, preparatory treatment and sweating during the anæsthetic period, were taken into consideration; the first count was made before the concentration. In Series D, Cases 17 and 24 show that the equilibrium existing between the plasma and the corpuscles was being restored, for the reason that the first blood counts were made prior to the preparatory treatment; the figures may even represent an absolute loss of chromocyte. In Series A, the average gain of 265,000 corpuscles appears to represent the degree of concentration over the inspissation induced by the preparatory measures produced during the anæsthetic period. In Series B, the average gain of 460,204 cells per cubic millimetre represents the degree of concentration produced during the anæsthesia and the postanæsthetic period.

In Series C the average gain of 740,000 cells per cubic millimetre represents the concentration produced by the preparatory measures of treatment and the anæsthetic period. It will be noticed that the average gain in Series C is greater than in any of the other groups. The explanation for this is probably that the period preceding the operation and the anæsthetic stage produced the highest degree of inspissation. In Series D, the average gain was 520,000 per cubic millimetre. This increase in the number of corpuscles represents the degree of inspissation produced by the three periods. It is apparent, however, that this gain is not so striking as the gain in Series C, probably for the reason that blood dilution has been active in some of the cases before the last examination.

Hæmoglobin.—The hæmoglobin gain and loss, when analyzed in regard to the four periods, A, B, C, and D, show varying results. In some instances the hæmoglobin is decreased; this necessarily represents an absolute decrease. When the total blood volume is fluctuating, the gain and loss of hæmoglobin are best determined by studying the individual corpuscular value in hæmoglobin.

Color Index.—The loss in the color index in Series A, namely, in that series in which the blood was examined just before and just after the anæsthetic stage, the color value was reduced in all but one instance. The average loss of color index in this series was .077. This seems to demonstrate clearly that there was marked blood destruction and increased blood production during the period of anæsthesia, as indicated by the loss in the average, the newly formed erythrocytes being deficient in coloring matter. Although the blood was concentrated, the individual hæmoglobin value fell.

In every instance in Series B the color index was reduced. The average loss of color value was .084. The average loss in Series B was more marked than the average loss in Series A. The reason for this is probably that rapid hæmogenesis of cells deficient in hæmoglobin progressed over a longer period, as the second blood count was made some time

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after the termination of the anæsthetic state. Therefore, the average color-value reduction was more pronounced.

In Series C, the average loss of color index was .097.

In Series D, the loss in the blood decimal was most pronounced; the average fall was .102. The explanation of this marked decrease is the same as that given for the change in Series B, namely, that erythrocytic regeneration was further advanced.

The constant loss in the color index is the most convincing evidence of rapid blood destruction. This loss in the color value occurred in Groups A, B, C, and D. In only one instance, in Group A, was there a slight gain; in every other instance there was a loss in the corpuscular hæmoglobin value. If the blood disturbances were due simply to concentration, the rise and fall in the percentage of corpuscles and the percentage of hæmoglobin would have been parallel, and the color index would not have been changed. The reduction in the color value of the corpuscles suggests rapid hæmocytolysis and increased hæmogenesis.

TABLE IV.

Group A.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Duration of Operation.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
37.	90 minutes.	820,000		.091
41.	75 "	70,000		+slight.
13.	65 "	990,000		.203
6.	60 "	120,000		.026
9.	60 "		130,000	.052
36.	38 "	635,000		.02
29.	37 "	420,000		.104
40.	35 "		210,000	.024
18.	30 "	660,000		.032
45.	30 "		470,000	.059
44.	25 "	450,000		.09
49.	25 "	200,000		.105
8.	24 "	170,000		.084
10.	23 "	430,000		.132
7.	12 "	25,000		.00

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Group B.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOME TIME AFTER ANÆSTHESIA.

Number.	Duration of Operation.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
19.	90 minutes.		290,000	.002
33.	83 "	600,000		.219
50.	73 "	140,000		.038
30.	67 "	1,305,000		.034
26.	65 "	90,000		.129
28.	65 "	700,000		.082
32.	60 "	1,140,000		.035
42.	55 "	380,000		.213
25.	48 "	1,210,000		.026
34.	45 "	930,000		.058
35.	45 "	680,000		.162
46.	45 "	1,160,000		.11
11.	40 "		260,000	.001
43.	40 "	480,000		.201
22.	38 "	690,000		.065
38.	30 "		750,000	.008
23.	28 "	820,000		.118
12.	27 "	12,500		.174
27.	25 "	317,000		.040
47.	25 "	420,000		.081
48.	20 "	240,000		.098
14.	18 "		170,000	.022

Group C.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Duration of Operation.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
21.	105 minutes.	240,000		.008
5.	55 "	30,000		.005
16.	19 "	1,550,000		.278

Group D.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOME TIME AFTER ANÆSTHESIA.

Number.	Duration of Operation.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
3.	120 minutes.	535,000		.147
4.	120 "	1,110,000		.10
20.	95 "	1,215,000		.136
15.	90 "	150,000		.073
39.	90 "	160,000		.149
17.	60 "		260,000	.071
2.	47 "	1,220,000		.158
1.	35 "	675,000		.13
24.	35 "		80,000	.036
31.	25 "	480,000		.018

BLOOD CHANGES INDUCED BY ETHER.

TABLE V.

Group A.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Amount of Ether used.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
18.	270 cubic centimetres.	660,000		.032
29.	270 "	420,000		.104
41.	255 "	70,000		+slight.
9.	6.0 "			
	180 "		130,000	.052
37.	240 "	820,000		.091
6.	210 "	120,000		.026
36.	165 "	635,000		.02
13.	7.8 "			
	144 "	990,000		.203
10.	150 "	430,000		.132
40.	150 "		210,000	.024
45.	150 "		470,000	.059
8.	135 "	170,000		.084
49.	120 "	200,000		.105
44.	75 "	450,000		.09
7.	7.2 "			
	45 "	25,000		.06

Group B.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOME TIME AFTER ANÆSTHESIA.

Number.	Amount of Ether used.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
33.	405 cubic centimetres.	600,000		.219
32.	360 "	1,140,000		.035
11.	240 "		260,000	.001
26.	240 "	90,000		.129
43.	240 "	480,000		.201
50.	240 "	140,000		.038
19.	225 "		290,000	.002
22.	195 "	690,000		.065
42.	195 "	380,000		.213
25.	180 "	1,210,000		.026
28.	180 "	700,000		.082
34.	154 "	930,000		.058
30.	143 "	1,305,000		.034
12.	7.2 "			
	128 "	12,500		.174
23.	135 "	820,000		.118
38.	120 "		750,000	.008
27.	105 "	317,000		.040
40.	90 "	1,160,000		.11
47.	90 "	420,000		.081
48.	75 "	240,000		.098
14.	6.0 "			
	45 "		170,000	.022
35.	30 "	680,000		.162

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Group C.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOON AFTER
ANÆSTHESIA.

Number.	Amount of Ether used.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
21.	330 cubic centimetres.	240,000		.008
5.	188 " "	30,000		.005
16.	103 " "	1,550,000		.278

Group D.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOME TIME AFTER
ANÆSTHESIA.

Number.	Amount of Ether used.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
3.	720 cubic centimetres.	535,000		.147
39.	330 " "	160,000		.149
1.	195 " "	675,000		.13
20.	180 " "	1,215,000		.136
2.	165 " "	1,220,000		.158
4.	165 " "	1,110,000		.10
31.	150 " "	480,000		.018
24.	120 " "		80,000	.036
17.	105 " "		260,000	.071
15.	75 " "	150,000		.073

The Duration of Operation and the Quantity of Ether employed.—The results do not seem to show any direct relationship between the blood disturbance and the duration of the operation. A similar statement may be made in regard to the quantity of ether. Of course, it is obvious that a prolonged operation upon a sound and vigorous patient will be tolerated better than even a brief operation upon one who is weak and exhausted; and also that some individuals will have much less blood destruction from the exhibition of a large quantity of ether than others will from inhaling a small quantity. On account of the many modifying factors, it is very difficult to determine the exact influence which the quantity of ether and the duration of the operation have upon the blood changes.

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TABLE VI.

Group A.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Blood Loss.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
6.	150 cubic centimetres.	120,000		.026
41.	120 " "	70,000		+slight.
9.	90 " "		130,000	.052
18.	90 " "	660,000		.032
49.	90 " "	200,000		.105
7.	30 " "	25,000		.06
8.	15 " "	170,000		.084
37.	15 " "	820,000		.091
13.	Small amount.	990,000		.203
10.	Minimum.	430,000		.132
29.	Bloodless.	420,000		.104
36.	"	635,000		.02
40.	"		210,000	.024
44.	"	450,000		.09
45.	"		470,000	.059

Group B.

BLOOD EXAMINATIONS MADE A SHORT TIME BEFORE AND SOME TIME AFTER ANÆSTHESIA.

Number.	Blood Loss.	Corpuscular Gain	Corpuscular Loss.	Loss of Color Index.
11.	120 cubic centimetres.		260,000	.001
19.	120 " "		290,000	.002
48.	120 " "	240,000		.008
26.	90 " "	90,000		.129
22.	60 " "	690,000		.065
35.	60 " "	680,000		.162
42.	60 " "	380,000		.213
47.	60 " "	420,000		.081
23.	30 " "	820,000		.118
25.	30 " "	1,210,000		.026
28.	30 " "	700,000		.082
38.	30 " "		750,000	.008
46.	30 " "	1,160,000		.11
50.	30 " "	140,000		.038
43.	15 " "	480,000		.201
32.	15 " "	1,140,000		.035
12.	Small.	12,500		.174
33.	"	600,000		.219
34.	Little.	930,000		.058
30.	Very slight.	1,305,000		.034
14.	Bloodless.		170,000	.022
27.	"	317,000		.040

Group C.

BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOON AFTER ANÆSTHESIA.

Number.	Blood Loss.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
21.	240 cubic centimetres.	240,000		.008
5.	50 " "	30,000		.005
16.	15 " "	1,550,000		.278

*Group D.*BLOOD EXAMINATIONS MADE SOME TIME BEFORE AND SOME TIME AFTER
ANÆSTHESIA.

Number.	Blood Loss.	Corpuscular Gain.	Corpuscular Loss.	Loss of Color Index.
3.	473 cubic centimetres.	535,000		.147
4.	300 " "	1,110,000		.10
20.	240 " "	1,215,000		.136
2.	90 " "	1,220,000		.158
24.	60 " "		80,000	.036
15.	30 " "	150,000		.073
39.	30 " "	160,000		.149
31.	15 " "	480,000		.018
1.	Slight.	675,000		.13
17.	Very little.		260,000	.071

Blood Loss.—The blood loss was very slight in nearly all of the cases, and in some there was practically no loss at all (eye operations). It appears that the amount of blood lost did not affect the blood changes to a perceptible degree. In Cases 7, 9, and 13 in Group A, and Cases 12 and 14 in Group B, chloroform was used in conjunction with the ether. The amount of chloroform employed was very small.

Animal Experiments.—The constant fall in the color index after anæsthesia suggested the idea of experimental study in this line. It is our intention to continue this work from an experimental stand-point. We feel that the single experiment which has been performed is worthy of mention, although we do not attempt to draw any positive conclusions from a solitary observation. Two rabbits were obtained, almost identical in point of age, size, and appearance. One animal was etherized for two hours and twenty minutes, 150 cubic centimetres of ether being employed during the anæsthetic period.

A blood examination ten minutes prior to the beginning of the etherization showed 6,140,000 erythrocytes per cubic millimetre, 79 per cent. of hæmoglobin, and a color index of .693. The second blood count was made thirty-nine minutes after the beginning of the inhalation of the ether. This examination showed 6,260,000 erythrocytes, 69 per cent. of hæmoglobin, and a color index of .592. The third examination was made one hour and fifty minutes after the beginning of

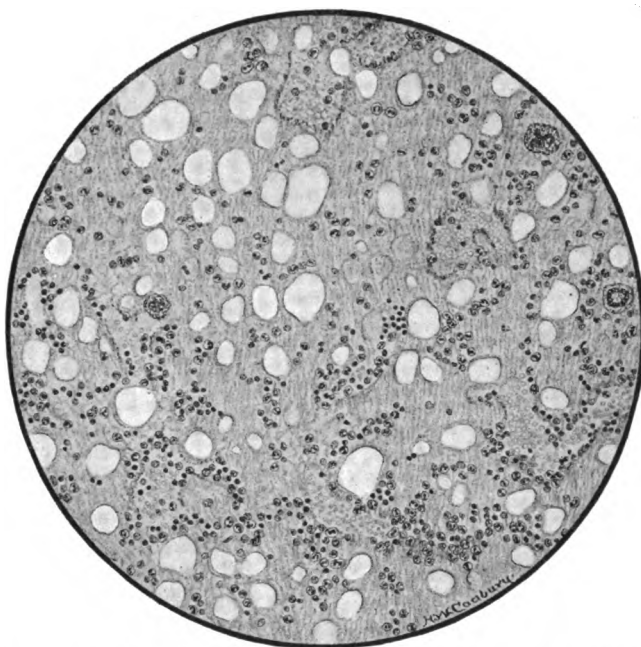


FIG. 1.—Section of normal bone marrow of femur (of rabbit).

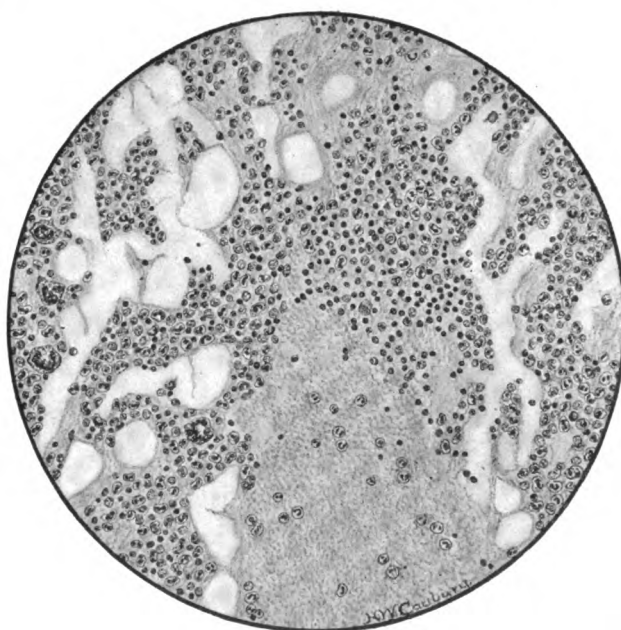


FIG. 2.—Section of bone marrow of femur (of rabbit) showing marked erythroblastic proliferation after death by etherization.

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the etherization; this count showed 7,000,000 erythrocytes, 69 per cent. of hæmoglobin, and a color index of .485. The animal was then killed with ether.

A Summary of the Post-Mortem Examination.—The serous cavities did not contain free fluid. The bladder contained a considerable quantity of urine, and the lower portion of the intestinal canal contained much thin fæcal matter. The spleen was small. The bone marrow of the right femur was bright red. Sections of the femur marrow were fixed in Gulland's formalin solution (formalin, 10 per cent., in absolute alcohol). They were dehydrated in alcohol and infiltrated in paraffin. The cut sections were stained with Ehrlich's triple stain—diluted with four times its volumes of water—for five minutes; washed in water; then treated for a few seconds with methylic alcohol; dehydrated in alcohol; cleared in xylol; and mounted in Canada balsam.

The other animal was killed by fracturing the spine. Upon post-mortem examination all of the serous cavities contained a small amount of fluid. The bone marrow of the right femur was not so red as was the marrow of the etherized animal, and was somewhat firmer. Pieces of this marrow were treated in a manner similar to the marrow of the etherized animal. Upon microscopic examination, by contrasting the marrow of the etherized animal and that of the non-etherized, it appears that in the former instance there is a marked cell proliferation, the cells being very numerous, and encroaching upon the normal fat spaces of the marrow. The cell proliferation in the marrow of the etherized rabbit involves particularly the erythroblastic elements; these cells are very numerous.

As previously stated, we hesitated to draw any conclusion from this single experiment; but, nevertheless, the very marked changes that were found are suggestive of the erythroblastic proliferation as a result of the ether. In the light of this experiment, it might be well to inquire whether the pains in the limbs and back, so common after anæsthetization, are not due, at least in part, to changes in the marrow. We must not omit to mention that the blood for examination was taken

from the ear; and that during the entire anæsthetic state only a trivial amount of blood was lost.

CONCLUSIONS.

(1) The number of red corpuscles is influenced by many factors associated with and accompanying the anæsthetic state. The character of this change is, as a rule, a polycythæmia; rarely, an oligocythæmia. These factors associated with and accompanying the anæsthetic state may be grouped into three classes. In each class when analyzed separately is found a cause capable of producing an increase in the number of colored corpuscles.

(2) The nature of this polycythæmia seems best explained by a lessening of the watery elements of the plasma, thereby reducing the total volume of the liquor sanguinis, and consequently causing concentration of the blood. It seems reasonable to infer that the polycythæmia is not influenced by excessive proliferative changes, which probably occur in the hæmatopoietic tissues. The increased blood production is an effort of nature to rapidly restore the destroyed cells.

(3) The three important factors incident to the polycythæmia are: (a) The period of preparatory operative treatment; (b) the anæsthetic state; and (c) the postoperative stage.

(4) The blood inspissation is, as a rule, most pronounced immediately after the termination of the anæsthetic stage. (See Group C.) In some instances the anhydræmia may be increased by each succeeding factor, or one of these factors may exceed the other; for example, the preparatory measures may bring about such a high grade of concentration that during the anæsthesia the polycythæmia may be stationary, or in a few hours may lessen somewhat. This variation existing between the plasma and the corpuscles, although temporary (for the economy adjusts the balance of the output and the intake of the watery principles of the blood with wonderful rapidity), should be regarded as too pronounced to be within the physiological limits. The relative increase in the number

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of erythrocytes is generally still present some time after the operation. (See Group D.) But not infrequently the adjustment of the watery and solid elements manifests itself before this time, and an oligocythæmia may be present.

(5) The hæmoglobin is always reduced absolutely; in some instances there is an apparent increase, but this rise in the percentage of hæmoglobin is never parallel with the rise in the number of red blood-cells. The individual corpuscular hæmoglobin value is therefore reduced. This reduction in the color value of the chromocytes is most striking when the color index, ascertained some time before the operation, is compared with the blood decimal, determined some time after the operation. We must conclude that etherization produces increased hæmolysis; and in nature's effort to rapidly replace the destroyed corpuscles the regenerated cells are imperfectly supplied with hæmoglobin.

(6) The duration of the anæsthetic state and the amount of ether may influence the blood changes; but the extent of the disturbances could not be determined on account of the many modifying factors.

(7) The amount of blood loss, as encountered in this series of cases, does not seem to affect the blood.

(8) Whenever possible, one or more blood examinations should be made before giving a general anæsthetic; and the examinations should be made before preparatory treatment has been instituted. On account of the hæmolysis, which is shown by the fall in corpuscular hæmoglobin after operation, a very low percentage of hæmoglobin must be regarded as a contraindication to the administration of a general anæsthetic. The amount which should be regarded as a positive contraindication is uncertain. We think, with Hamilton Fish, that below 50 per cent. is a dangerous level. In malignant disease, and in cases where surgery might prolong life briefly but cannot cure, operation should not be performed under a general anæsthetic if hæmoglobin is below 50 per cent. We have operated in two cases in which the hæmoglobin was 40 per cent.; in each instance a vital emergency existed, and in

each case death upon the table was narrowly averted. Mikulicz sets 30 per cent. as the lowest level at which operation is to be attempted. We must not give a general anæsthetic, except under the stress of absolute necessity, if the hæmoglobin is below 40 per cent. It is true that cases are occasionally anæsthetized with success when there is less than 40 per cent.; we know of one case with 30 per cent., and another with 24 per cent.; but a few exceptions do not disprove the rule. If there is a low percentage of hæmoglobin local anæsthesia should be employed whenever it is possible.

Whenever the percentage of hæmoglobin is low, if an operation is determined upon, the ordinary preparatory measures should be modified in every way, in order to avoid creating an undue drain upon the blood. If a general anæsthetic is given, its administration should be intrusted to an experienced man; as little as possible should be given; in many instances oxygen should be combined with it; the operation should be performed rapidly; proper measures should be taken to bring about reaction after its completion, and oxygen should be inhaled to remove the ether quickly from the lungs and blood.

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THE ACTUAL AND COMPARATIVE RESISTANCE OF ACID-FAST BACILLI.*

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[From the Laboratories of the Jefferson Medical College Hospital.]

No more interesting group of bacteria has ever been isolated than that which is known as the acid-fast group. It comprises quite a few organisms, among them being some isolated from butter, some from milk, others from grass; while the lepra bacillus, the smegma bacillus, the bacillus of syphilis (Lustgarten), and the tubercle bacillus are also included in the group.

All of these have been successfully cultivated and studied, with the possible exceptions of the bacillus of leprosy, the bacillus smegmatis, and the so-called bacillus of syphilis. The latter organisms are claimed by some to have been cultivated, but by most observers these assertions are denied.

Courmont and Potet¹ have tabulated a list of acid-fast bacilli as regards their origin:

- | | |
|-------------------------------|---|
| 1. (A) <i>Pathogenic.</i> | <i>In Animals.</i> |
| B. tuberculosis. | 1. Human, avian, bovine, and piscum t. b. |
| B. lepra. | 2. B. Moeller. |
| (B) <i>Non-pathogenic.</i> | 3. Calves' smegma. |
| (a) Upon the lips. | 4. Mist. B. |
| (b) B. smegmatis. | <i>In Butter.</i> |
| (c) B. cerumen. | (a) Petri Rabinowitsch. |
| (d) B. nasal mucus. | (b) Korn. |
| 2. <i>In Diseases of Man.</i> | (c) B. Coggi. |
| (a) Gangrene of lung. | (d) B. Tobler (i, ii, iii, iv, v). |
| (b) Conjunctivitis. | (e) B. Markl. |
| (c) Genito-urinary diseases. | (f) B. Minot. |
| (d) Fæces from typhoid. | (g) Moeller's milk B. |
| (e) Leprosy. | <i>In Nature.</i> |
| (f) Tuberculosis. | 1. Upon Plants: |
| | (a) Timothy B. Moeller. |
| | (b) Grass B. Moeller. |
| | 2. In Earth: |
| | (a) Sewage (Spina-Houston). |
| | (b) Earth (Karlinski-Moeller). |
| | 3. Mist. B. |

*Read before the Pathological Society of Philadelphia, Dec. 10, 1903.

¹*Archiv. Méd. de Expér.*, vol. xv, Jan. 1, 1903, p. 83.

The resemblances these organisms possess are principally in morphologic and tinctorial properties, the cultures differing very markedly as regards the time of appearance of the growth after inoculation.

Moeller² regards the butter and milk bacilli which are resistant to acids as varieties of the grass bacilli 2, in consideration of the fact that they have a common habitat. He also cultivated from milk in pure culture an organism which he has named the timothy bacillus. It is a slender rod, sometimes slightly curved, which microscopically is often impossible to distinguish from the tubercle bacillus. In the decolorizing solution, as well as in sections with the ordinary staining methods, it behaves exactly like the tubercle bacillus.

Besides these organisms he mentions a "manure bacillus," which bears a morphologic and tinctorial resemblance to the timothy bacillus. In growth of cultures and in pathogenesis it also resembles the grass bacillus 2.

Grassberger, Korn, and others have isolated acid-resisting bacilli from butter and grass.

Capaldi isolated a bacillus from cow's dung which resembled the Petri Rabinowitsch butter bacillus. Severin found similar bacilli in horses' dung; Ferran in cows', horses', and human feces. Acid-resisting bacilli have also been encountered in the human intestine by von Jaksch.

Novy mentions acid-resisting bacteria occurring in the conjunctiva.

Alvarez and Tavel were the first to observe an acid-resisting bacillus in smegma, and called it the bacillus smegmatis. Laser and Czoplewski claim to have obtained this organism upon artificial culture media.

Cowie,³ in making observations upon the smegma bacillus of man and also of the lower

²*Lancet*, July 27, 1901, pp. 204-5.

³*Journal of Experimental Medicine*, 1900, vol. v, p. 205.

animals, finds that acid-resisting bacilli are found in the smegma of the horse, cow, dog, guinea-pig, and white rat. In the rabbit and cat no such organisms exist. He claims that the human smegma bacillus resists a 25-per-cent solution of nitric acid for ten minutes; absolute alcohol decolorizes the organism in ten seconds.

He quotes Zahn as noticing the presence in non-tuberculous sputum of acid-resisting bacilli; while A. Fraenkel and Rabinowitsch observed acid-fast bacilli in sputum from cases of pulmonary gangrene. Moeller also found acid resisting bacilli in non-tuberculous sputum.

Ophüls⁴ reports five cases of gangrene of the lung, in the lesions of which acid-proof bacilli were found. In the first case the bacilli were slender, stained irregularly, arranged in short threads with true branching. The organisms were frequently arranged in dense clusters and stained poorly with methylene blue, better in dilute carbol fuchsin and by Gram's method. They were decolorized by a one-per-cent solution of hydrochloric acid in 60-per-cent alcohol. When sections were treated with 25-per-cent sulphuric acid and mounted in glycerin in order to avoid the alcohol, they remained stained. They stained better when a 12½-per-cent solution of sulphuric acid was used. They were not obtained in culture. Glycerin agar-agar was the only medium used for inoculations.

In the second case bacilli were found which resembled very much those found in Case 1. These bacilli grew upon glycerin agar in the form of moist, grayish-white colonies for the first generation, but no further growth could be obtained while under aerobic or anaerobic conditions.

In the third case large numbers of acid-proof

⁴*Journal of Medical Research*, vol. viii, No. 1, p. 242.

bacilli were observed. On the walls of the cavity the organisms grew in the form of S-shaped bunches very much like the tubercle bacillus. The bacilli did not grow on ordinary media.

The fourth case also showed in the areas of disease and in spreads acid-proof bacteria. They were not obtained in culture.

In the fifth case acid-proof bacilli were found in the diseased areas, which organisms resembled those found in the four previous cases. They were not obtained by ordinary methods of cultivation.

Benvenuti⁵ found in the sputum of a case of pulmonary gangrene acid-proof bacilli which were mistaken for tubercle bacilli. Post-mortem examination showed, however, a complete absence of tubercular lesions.

Mayer⁶ in fifty-eight cases of gangrene of the lung, found in the sputum of ten acid-proof bacilli which were not tubercle bacilli, and which he classifies as streptothrices. He also obtained them in culture; the growth being a wrinkled, white layer. They were not pathogenic for animals.

Foli⁷ in six cases of gangrene of the lung, found acid-fast bacilli in three. He was able to differentiate the true tubercle bacillus from the acid-fast organisms by means of a solution of tartaric acid (1:20). (Whether an alcoholic or watery solution is not stated.) He claims that the "pseudo-tubercle bacilli" decolorize in five minutes, while the true tubercle bacillus requires twenty minutes for its decolorization.

The bacillus of avian tuberculosis resists acids and differs from the mammalian tubercle bacillus in the appearance of cultures and the temperature conditions, thriving well at 42° C., while the organism of mammalian tuberculosis does not.

⁵*Gaz. degli Osped. edelle clin.*, 1900, No. 141.

⁶*Münchener med. Woch.*, 1901, 1775.

⁷*Riv. Med.*, Aug. 27, 1901.

The bacilli of fish and bovine tuberculosis also resist acids, the latter more markedly than the former.

Klein and Marmorek have shown that all tubercle bacilli are not acid-fast, as in young bacilli which have not yet been covered with the peculiar fatty matter found in older bacilli decolorization takes place with acid solutions.

Borrel claims that after long action of warm xylol upon the tubercle bacillus, he separated a mass which was resistant to acids and alcohol, whilst the tubercle bacilli thus treated lost their acid-fast properties.

Abbott and Gildersleeve,⁸ in an article upon the etiological significance of the acid-resisting group of bacteria, remark that all of these bacilli resist "for longer or shorter periods" solutions of acids. For example, they resist "5 per cent acetic acid and alcohol, hydrochloric acid 3 per cent and alcohol, sulphuric acid 5 per cent in water, but are decolorized almost instantly if treated with nitric acid 25 to 30 per cent."

Pseudo-tubercle bacilli have been found not only in sputum, but also in mucus from the nose and pharynx, coating of the tongue, sordes on the teeth, as well as in the secretion upon the tonsils.

Rappin and Henrot⁹ in four cases of syphilis isolated a bacillus in the urine, very pleomorphic, and possessing acid-fast properties, resembling the bacillus of Lustgarten.

Macé claims that the smegma bacillus will not resist glacial acetic acid for two minutes, but the human tubercle bacillus will. If the *B. smegmatis* is treated with a 5-per-cent solution of caustic soda in alcohol the acid-fast property is lost, but this property is said not to be affected in the *B. tuberculosis*. These facts the writer can fully substantiate by the experiments included in the tables.

⁸*Univ. of Penna. Med. Bulletin*, June, 1902.

⁹*Soc. de Biologie*, vol. 55, March, 1903, p. 408.

Bulloch,¹⁰ in speaking upon the acid-fast properties of the tubercle bacillus, mentioned that it was also alcohol-fast, and that these properties (acid- and alcohol-fast) were not due to the presence of fat in the bacillus, but to a body of a waxy nature which, when removed from the bacillus with boiling chloroform or boiling benzine, was in itself powerfully acid-fast, and unstainable by fat stains (Aronson). Besides wax and fat, which were present in relatively large amount, the tubercle bacillus was composed of proteids (important among which was a variety of nucleic acid described as tuberculinic acid, Ruppel) and salts, with phosphate predominating. After the removal of all proteids, wax, and fat, a substance remained which contained a considerable quantity of nitrogen, and from its reactions was probably chitin or some allied body.

In this communication the writer presents a series of experiments, determining the actual resistance of the acid-fast bacilli to mineral acids and other reagents.

In the first experiments (Table I) spreads were made from three-weeks-old cultures of the organisms, excepting the smegma bacillus. The spreads were dried, fixed, and stained for fifteen minutes with carbol fuchsin, heating the cover-slip slightly during this time. They were next washed with water, then the reagent applied from fifteen to thirty minutes. In most of the preparations fifteen minutes was the maximum time limit, while some actually resisted the reagents forty-five minutes. The same technique was also resorted to in using aniline gentian violet, with practically the same results as those obtained with carbol fuchsin.

It will be seen that with sweet spirits of nitre and glacial acetic acid (full strength) all organisms were decolorized with the exception of the

¹⁰*Lancet*, July 27, 1901, p. 243.

bacillus of human, bovine, and avian tuberculosis.

With 20-per-cent nitric acid all were decolorized, with the exception of the bacilli of human and bovine tuberculosis and the smegma bacillus. They all resisted 25-per-cent sulphuric acid with the exception of the grass bacillus (Korn 1) and the milch bacillus. Besides the margarin bacillus, grass bacillus (Moeller 2), and blindschleichen bacillus, they all resisted 30-per-cent sulphuric acid. With 40-per-cent sulphuric acid they were all decolorized with the exception of the bacilli of human, bovine, and avian tuberculosis, Karlinski's bacillus, and the horse-dung bacillus. With 30-per-cent hydrochloric acid, the bacillus of fish tuberculosis, Grassberger's butter bacillus, Korn's grass bacilli Nos. 1 and 2, and the smegma bacillus were decolorized. With absolute alcohol only the smegma bacillus was decolorized. Twenty-per-cent sulphurous acid failed to decolorize any, even after thirty minutes' application.

Tartaric acid (1:20) in watery as well as alcoholic solution of same strength failed to decolorize any of the organisms.

TABLE I.

Carbol fuchsin.	Spt. eth. nitrosi.	20% HNO ₃ .	30% HCl.	25% H ₂ SO ₄ .	30% H ₂ SO ₄ .	40% H ₂ SO ₄ .	Absolute alcohol.	Glacial acetic acid.	20% H ₂ SO ₃ .	1-20 tartaric acid.
Human T. B.....	++	++	+	++	++	++	++	++	++	++
Bovine T. B.....	++	++	+	++	++	++	++	++	++	++
Avian T. B.....	++	++	++	++	++	++	++	++	++	++
Piscium T. B.....	++	++	++	++	++	++	++	++	++	++
Butter B. Rabinowitsch	++	++	++	++	++	++	++	++	++	++
Butter B. Grassberger....	++	++	++	++	++	++	++	++	++	++
Margarin B.....	++	++	++	++	++	++	++	++	++	++
Grass B. Korn 1.....	++	++	++	++	++	++	++	++	++	++
Grass B. Korn 2.....	++	++	++	++	++	++	++	++	++	++
Grass B. Moeller 1.....	++	++	++	++	++	++	++	++	++	++
Grass B. Moeller 2.....	++	++	++	++	++	++	++	++	++	++
Milch B.....	++	++	++	++	++	++	++	++	++	++
Horse-dung B.....	++	++	++	++	++	++	++	++	++	++
Milch B.....	++	++	++	++	++	++	++	++	++	++
Blindschleichen B.....	++	++	++	++	++	++	++	++	++	++
Karlinski's B.....	++	++	++	++	++	++	++	++	++	++
Smegma B.....	++	++	++	++	++	++	++	++	++	++

+ Resistance to. — Decolorized by.

The next experiments were made by boiling in xylol spreads of the organisms. They were then stained with carbol fuchsin and afterward treated with 25-per-cent sulphuric acid; all resisted except Korn's grass bacillus No. 1, the milch bacillus, and bacillus smegmatis.

Spreads were then boiled in a 5-per-cent aqueous solution of sodium hydrate, stained as before and treated with 25-per-cent solution of sulphuric acid, with the result that all decolorized with the exception of the bacilli of bovine and human tuberculosis. If the bacillus of human and bovine tuberculosis and the smegma bacillus are treated with sodium hydrate and then with 25-per-cent nitric acid, they will be completely decolorized. If a 5-per-cent alcoholic solution of sodium hydrate is used and spreads of the human tubercle bacillus and the smegma bacillus stained with carbol fuchsin and afterward treated with 25-per-cent solution of sulphuric acid, the smegma bacillus is decolorized, while the human tubercle bacillus still retains the dye.

TABLE II.

	Xylol followed by 25% sol. H_2SO_4 .	5% aqueous sol. NaOH followed by 25% H_2SO_4 .	5% aqueous sol. NaOH followed by 25% HNO_3 .
Human tubercle B.....	+	+	-
Bovine tubercle B.....	+	+	-
Avian tubercle B.....	+	+	-
Fish tubercle B.....	+	+	-
Butter B. Rabinowitsch.....	+	+	-
Butter B. Grassberger.....	+	+	-
Margarin B.....	+	+	-
Grass B. Korn 1.....	-	-	-
Grass B. Korn 2.....	+	+	-
Grass B. Moeller 1.....	+	+	-
Grass B. Moeller 2.....	+	+	-
Mist B.....	+	+	-
Horse-dung B.....	+	+	-
Milch B.....	-	-	+
Blindschleichen B.....	+	+	+
Karlinski's B.....	+	+	-
Smegma B.....	-	-	-

The next series of experiments were upon spreads of fresh sputum containing tubercle bacilli, spreads made from sputum preserved in Strohschein's solution for eighteen months,

and spreads of smegma. These were treated in various ways, as will be seen by the appended table. The interesting point is that the tubercle bacillus retains its acid-resisting properties for an indefinite time in a preserving solution.

The latter series of experiments shows how long the tubercle bacillus resists acids. The fact that numerous observers have found acid-fast bacilli in the sputum and in the parenchyma in cases of gangrene of the lungs, would lead one to suggest that these might represent dead or attenuated forms of the tubercle bacillus. Their decolorization with alcohol after the application of acid would, however, negative this view.

TABLE III.

Spreads of fresh sputum.	Spreads of preserved sputum.	Spreads of smegma.
1. Xylol (boiled) carbol fuchsin—20% nitric acid. —	Xylol (boiled) carbol fuchsin—20% nitric acid. —	Xylol (boiled) carbol fuchsin—20% nitric acid. —
2. Xylol (boiled) carbol fuchsin—sweet spirits of nitre. +	Xylol (boiled) carbol fuchsin—sweet spirits of nitre. +	Caustic soda (5% aqueous solution) boiled—carbol fuchsin—20% nitric acid. —
3. Caustic soda (5% aqueous solution) boiled—carbol fuchsin—20% nitric acid. —	Caustic soda (5% aqueous solution) boiled—carbol fuchsin—20% nitric acid. —	Caustic soda (5% alcoholic solution) boiled—carbol fuchsin—20% nitric acid. —
4. Caustic soda (5% alcoholic solution) boiled—carbol fuchsin—20% nitric acid. —	Caustic soda (5% alcoholic solution) boiled—carbol fuchsin—20% nitric acid. —	Carbol fuchsin—40% sulphuric acid. —
5. Carbol fuchsin—glacial acetic acid (pure). +	Carbol fuchsin—glacial acetic acid (pure). +	Carbol fuchsin—sweet spirits of nitre. —
6. Caustic soda (5% aqueous solution) boiled in carbol fuchsin—glacial acetic acid (pure). —	Caustic soda (5% aqueous solution) boiled in carbol fuchsin—glacial acetic acid (pure). —	Ether (boiled) carbol fuchsin—20% nitric acid. —
7. Carbol fuchsin—40% solution sulphuric acid. +	Carbol fuchsin—40% solution sulphuric acid. +	
8. Ether (boiled in) carbol fuchsin—20% nitric acid. —	Ether (boiled in) carbol fuchsin—20% nitric acid. —	
9. Carbol fuchsin—1-20 tartaric acid (aqueous). +	Carbol fuchsin—1-20 tartaric acid (aqueous). +	
10. Carbol fuchsin—1-20 tartaric acid (alcoholic). +	Carbol fuchsin—1-20 tartaric acid (alcoholic). +	

As some observers have shown, in young cultures of the tubercle bacillus, some of the organisms decolorize with acids; the writer found the same condition in young cultures of the various acid-fast organisms studied.

In morphology some of these organisms may be taken for the human tubercle bacillus, but the majority of them were shorter, especially so in old cultures. Where a spread of milk or butter contains only one or two demonstrable acid-fast bacilli, it is then that some doubt may arise as to what organism we are dealing with.

Of course the best and seemingly the only way in very doubtful cases to differentiate these various organisms is to make cultural as well as inoculation experiments upon animals, when they can be readily told apart.

The growth of the butter, grass, and milk bacilli makes its appearance in thirty-six or forty-eight hours at ordinary room temperature, while that of the tubercle bacillus requires at least ten days at body temperature.

The fact should also be borne in mind that the butter and other bacilli grow upon plain agar, while the tubercle bacillus requires blood serum or glycerin agar.

Tartaric acid either in alcoholic or watery solution failed to decolorize any of the organisms, though Foli claims that with this solution he was able to differentiate the "pseudo-tubercle" bacillus in sputum from the true tubercle bacillus.

Watery mixtures of all the bacilli mentioned were made and treated with one-per-cent solution of osmic acid, to determine whether the fat of the organisms responded to this reagent. In all the sediment which collected at the bottom of the tubes was turned black. In hanging-drop preparations all the organisms were of a brownish tinge with the exception of Korn's grass bacillus No. 1 and Moeller's grass bacillus

No. 1. Spreads were then made, fixed and stained with carbol fuchsin, and treated with a twenty-five-per-cent solution of sulphuric acid. They were seen to still resist the acid.

It has been stated by Sebrazes (quoted below) that if sputum or any material containing tubercle bacilli was exposed to the action of nitric acid, the organism would then not respond to a stain, in fact lose its tingibility. Spreads of fresh sputum were made, one-half of the surface was paraffined and then placed in a one-per-cent solution of nitric acid for eighteen hours. This left one-half of the cover exposed to the acid solution. At the end of this time the paraffin was removed with xylol and the spread stained with carbol fuchsin, then treated with Gabbet's solution. It was seen that the bacilli stained as well as if no acid solution had been previously applied.

Sebrazes (*Ann. de l'Institut Pasteur*, April 25, 1903, p. 303) has experimented upon the colorability of the B. of Koch. Stain used, Ziehl-Neelsen. The staining is not influenced by distilled water; boiling water; anilin water, H_2O_2 —12 volumes; Lugol's solution; alcohol; ether; chloroform; xylol; benzine; acetic acid; sat. aq. sol. of boric acid; picric acid; carbolic acid; sat. alc. sol. of salicylic acid; ammonia; caustic soda; carbonate of sodium; sulphite of sodium; KI; sulphate of aluminum; sulphate of copper; chloride of barium saturated in water; bichloride of mercury 1:100 or 1:1000; cyanide of mercury 1:100 or 1:1000; creolin mixtures; Van Swieten's liquid; the reagents of Esbach and Fleming. The bacilli cannot be identified in sputum treated with nitric acid; HCl ; H_2SO_4 ; one-per-cent osmic; one-per-cent permanganate of potassium; bichloride of tin and nitrate of bismuth saturated in water; sulphide of ammonium; reagent of Boas; sulphomolybdic acid. The tingibility is slightly

affected by chromic acid, 2 per cent; formol; H_2SO_4 , 24 per cent in water for two days; sat. aq. sol. of acetate of lead; nitrates of barium and silver, one per cent; acid alcohol, two per cent; chromate and bichromate of potassium, saturated in water; alcoholic solution of phenolphthalein; the aceto-picric reagents of Fehling, Kleinenberg, Tauret, Uffelman; and tincture of iodine. The ferricyanide of potassium and nitroprussiate of sodium when brought in contact with Ziehl-Neelsen solution cause a precipitate of crystals that resemble tubercle bacilli.

The conclusions deduced from these few experiments are that in doubtful cases, where acid-fast bacilli are encountered, a diagnosis of tubercle bacilli can be positively made by after-treatment of the stained spread with sweet spirits of nitre or glacial acetic acid, as these two reagents completely decolorize other acid-fast organisms, as the grass and butter bacilli and the smegma bacillus. Inoculation experiments should always be made where only a few organisms are observed.

In conclusion I wish to extend my thanks to Dr. Ravenel for the various cultures used in the experiments.

REPORT
OF THE
LABORATORIES
OF THE
JEFFERSON MEDICAL COLLEGE HOSPITAL

For Five Years, Ending December 31st, 1902.

W. M. L. COPLIN, M. D., Director.

The following is a tabulated report of the work done in the Laboratories for five years, ending December 31st, 1902. The total number of specimens included in this report is 2051. Prior to 1900 the records are not fully satisfactory; the sputum, urine and gastric-contents examinations were indifferently classified, and since that date they have been indexed separately, deposited in the clinical files of the Hospital, and do not appear upon the Laboratory records. In addition to the official records herein tabulated, there are about 200 unofficial examinations which will be included in a subsequent paper, epitomizing and condensing the results given here in detail. The numbered examinations are continuous and hence it has been deemed unnecessary to page the report.

The following is a list of specimens and materials examined in the Laboratories during the year 1897 :

* The word "negative" is used in this report to mean (1) The material or body which the examination was conducted to demonstrate was not present. (2) No information of diagnostic importance was obtained. Thus a blood or urinary examination yielding no diagnostic aid is marked "negative". The same word is used when, for example, the Widal test was applied without the occurrence of clumping. The different applications will be apparent.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
59—Sputum, histologic and bacteriologic examination of.	Tuberculosis.	75—Sand for water filtration.	Report published elsewhere.*
60—Bouillon inoculation, to determine character of infection.	Staphylococcus infection.	76—Water for analysis, before and after filtration.	Report published elsewhere.*
61—Bouillon inoculation, to determine character of infection.	Mixed infection, Staphylococcus and bacillus pyogenes foetidus.	77—Urine.	Beginning Bright's disease.
62—Bouillon and agar inoculation, to determine character of infection.	Diplococcus pneumoniae.	78—Urine.	Beginning Bright's disease.
63—Pus, to determine character of infection.	Staphylococcus infection.	79—Ovary, for histologic diagnosis.	Adenoma.
64—Inoculation from heart blood, post-mortem, to determine character of infection.	No bacteria present.	80—Urinary calculus.	Phosphatic calculus.
65—Pus, to determine character of infection.	Staphylococcus infection.	81—Tumor of parotid region, for pathologic diagnosis.	Mixed cell sarcoma.
66—Swab from throat, case suspected to be diphtheria.	Proved not to be diphtheria.	82—Piece of hard palate, for pathologic diagnosis.	Squamous epithelioma.
67—Pus or contents of cyst of ovary, to determine character of infection.	Mixed infection, staphylococcus albus and bacillus coli communis.	83—Small piece of tissue from tongue, for pathologic diagnosis.	Papilloma.
68—Bouillon inoculations from post-mortem, case of surgical kidney, to determine character of infection.	Staphylococcus infection.	84—Pus and gall bladder, to determine character of infection.	Staphylococcus aureus and bacillus coli communis.
69—Sputum, to determine if case be one of tuberculosis.	Bacillus of tuberculosis found present.	85—Small growth from penis, for pathologic diagnosis.	Papilloma.
70—Culture tube inoculation, to determine character of infection.	Staphylococcus infection.	86—Chain of glands, for pathologic diagnosis.	Tuberculous lymphadenitis.
71—Culture tube inoculation, to determine character of infection.	Staphylococcus infection.	87—Small mass from cheek, for histologic diagnosis.	Cutaneous tuberculosis.
72—Tendon of kangaroo, to determine character of infection.	Sterile.	88—Agar inoculation, to determine character of infection.	Bacillus putrificus coli, staphylococcus aureus, (b) Bacillus coli communis.
73—Examination for action of P—s Odorless Disinfectant.	Fairly good deodorizer, but poor disinfectant.	89—Inoculated tubes, to determine character of infection.	Bacillus coli communis.
74—Swab from throat, to determine diphtheria.	Diphtheria.	90—Tumor of abdominal wall, for histologic diagnosis.	Mixed cell sarcoma.
		91—Mammary gland, for histologic diagnosis.	Scirrhus carcinoma.
		92—Cystic tumor of omentum, for pathologic diagnosis.	Mixed cell, alveolar, melanotic sarcoma.
		93—Piece of liver, for histologic diagnosis.	Gumma.

* Report published in the *Engineering News* in the serial consideration of Water Filtration, for 1898.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
94—Spleen, for histologic diagnosis.	Splenic hyperplasia.	115—Two tubes inoculated, to determine character of infection.	Sterile.
95—Scrapings from interior of uterus, for histologic diagnosis.	Cylindric cell epithelioma.	116—Shreds of tissue, for pathologic diagnosis.	Tuberculosis.
96—Recurrent tumor of face, for histologic diagnosis.	Tubulated epithelioma.	117—Wall of abscess, for pathologic diagnosis.	Tuberculosis.
97—Two agar tubes inoculated, to determine character of infection.	Sterile.	118—Tumor of omentum, for pathologic diagnosis.	Myxosarcoma.
98—Shreds of tissue from abscess of groin, for pathologic diagnosis.	Tuberculosis.	119—Blood examination, for malaria.	Examination negative.
99—Urine, to determine presence of tuberculosis of genito-urinary organs.	Unable to find tubercle bacilli.	120—Rectal tumor, for pathologic diagnosis.	Cylindric cell epithelioma.
100—Urine, to determine presence of tuberculosis of genito-urinary organs.	Unable to find tubercle bacilli.	121—Urine, to be examined for tubercle bacilli.	Examination negative.
101—Tumor from rectum, for pathologic diagnosis.	Cylindric cell carcinoma.	122—Tumor of thigh, for histologic diagnosis.	Myxosarcoma.
102—Urine, to determine renal inflammation.	Examination negative.	123—Foreskin from phymosis, evidence of cancer.	Negative.*
103—Urine, to determine renal inflammation.	Examination negative.	124—Gland from axilla, for pathologic diagnosis.	Acute lymphadenitis.
104—Portion of stomach, for pathologic diagnosis.	Columnar epithelioma of pylorus.	125—Tissue removed from neck, for pathologic diagnosis.	Inflammatory tissue.
105—Urine, for pathologic diagnosis.	Purulent cystitis.	126—Growth from nose, for pathologic diagnosis.	Inflammatory mass.
106—Two tubes inoculated, to determine character of infection.	Sterile.	127—Tumor from rectum, for pathologic diagnosis.	Tubulated adenoma.
107—Tumor of superior maxilla (left), for pathologic diagnosis.	Squamous cell epithelioma of antrum.	128—Piece of gastric ulcer, stomach, and intestines, for pathologic diagnosis.	Cylindric cell cancer of stomach with secondary metastasis
108—Growth from gum of upper jaw (epulis), for pathologic diagnosis.	Giant cell sarcoma.	129—Part of stomach wall, for pathologic diagnosis.	Cylindric cell cancer.
109—Part of lower jaw, for pathologic diagnosis.	Squamous cell epithelioma.	130—Culture tube inoculation, to determine character of infection.	Sterile.
110—Tumor of upper jaw, for pathologic diagnosis.	Giant cell sarcoma.	131—Small piece of placenta, to be examined for evidence of syphilis.	Examination negative.
111—Pus from wound in abdominal wall, to determine character of infection.	Mixed infection, staphylococcus aureus and diplococcus pneumoniae.	133—Tissue removed from back of neck, for pathologic diagnosis.	Inflammatory induration.
112—Small gland from omentum, for pathologic diagnosis.	Mass of inflammatory tissue.	134—Two warts, for pathologic diagnosis.	Simple and pigmented papillomata.
113—Two tubes inoculated, to determine character of infection.	Sterile.	135—Wart from finger, for pathologic diagnosis.	Papilloma.
114—Two tubes inoculated, to determine character of infection.	Sterile.	136—Three culture tubes and small piece of mesenteric gland, to determine character of infection.	Mixed infection, Bacillus coli communis, micrococcus foetidus staphylococcus pyogenes albus and pyogenes aureus.
		137—Culture from appendix, to determine character of infection.	Bacillus coli communis, staphylococcus pyogenes albus.

The following is a list of specimens and materials examined in the laboratories during the year 1898 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
138—Three tubes of blood from lumbar puncture, to determine character of infection.	Mixed infection. Micrococcus pyogenes aureus; Bacillus subtilis; Bacillus gracilis.	165—Tumor from ear, for histologic diagnosis.	Fibrous polyp.
139—Blood examination.	Symptomatic anemia.	166—Fluid drawn from pleural cavity, to determine character of infection.	Mixed infection. Staphylococcus, and diplococcus.
140—Sputum, for tubercle bacilli.	Not present.	167—Urine.	Negative.*
141—Blood, (a) complete examination, (b) for malaria organisms.	(a) Symptomatic anemia. (b) No malarial organisms found.	168—Sputum, for tubercle bacilli.	Present.
142—Tumor, for histologic diagnosis.	Scirrhus carcinoma.	169—Soap, antiseptic, to be tested	Strongly antiseptic.
143—Urine.	Acute cystitis.	170—Tumor (?) of breast, for histologic diagnosis.	Post-inflammatory mammary fibrosis.
144—Urine.	Chronic parenchymatous nephritis.	171—Bladder and kidney.	Suppurative cystitis with secondary suppurative pyelonephritis.
145—Spleen and piece of kidney, for histologic diagnosis.	Supernumerary spleen showing infraction.	172—Blood, for Widal's reaction.	Positive.
146—Urine, for tubercle bacilli.	Not present.	173—Blood, for Widal's reaction.	Negative.*
147—Semen.	Spermatorrhœa.	174—Urine, for tubercle bacilli.	Not present.
148—Urine, for lead.	Not present.	175—Blood, for Widal's reaction.	Positive.
149—Growth from eyelid, for histologic diagnosis.	Cancer Squamous.	176—Culture tube inoculation, to be examined for actinomyces.	Not present.
150—Blood, for Widal's reaction.	Positive.	177—Urine, for blood.	None present.
151—Blood, for Widal's reaction	Negative *	178—Urine, for blood.	None present.
152—Blood, for Widal's reaction.	Negative.*	179—Culture tube inoculation, to be examined for the Bacillus typhosus.	Not present.
153—Sputum, for tubercle bacilli.	Not present.	180—Stomach and portion of liver for histologic diagnosis.	Carcinoma, cylindric cell.
154—Blood examination.	Negative.*	181—Urine, for microscopic examination.	Negative.*
155—Blood examination.	Negative.*	182—Blood, for Widal's reaction.	Positive
156—Culture tube inoculation, to determine character of infection.	No growth.	183—Urine.	Hematuria.
157—Blood examination.	Negative *	184—Urine.	Phosphaturia.
158—Blood examination.	Negative.*	185—Culture tube inoculation, to determine character of infection.	Spirillum concentricum.
159—Blood examination.	Negative.*	186—Intestine, for histologic diagnosis.	Examination pending.
160—Blood examination.	Symptomatic anemia.	187—Blood, for Widal's reaction.	Positive.
161—Blood, for Widal's reaction.	Positive.	188—Blood, for Widal's reaction.	Positive.
162—Urine, for tubercle bacilli.	Present.	189—Blood examination.	Negative.*
163—Culture tube inoculation, to determine character of infection.	Mixed infection. Bacillus diphtheriæ, micrococci.	190—Blood, for Widal's reaction.	Positive.
164—Urine.	Parenchymatous nephritis.	191—Fluid from right pleural cavity, for bacteriologic examination.	Negative.*
		192—Scrapings from tumor of elbow, for histologic diagnosis.	Inflammatory tissue.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
193—Urine, for tubercle bacilli.	Not present.	218—Sputum, for tubercle bacilli.	Not present.
194—Mass of tissue coughed up; histologic diagnosis.	Fibrinous pseudomembrane.	219—Culture tube inoculations, to determine character of infection.	Diplococcus pneumoniae.
195—Piece of tongue, for histologic diagnosis.	Tuberculosis.	220—Culture tube inoculations, to determine character of infection.	No bacteria found.
196—Tumor from groin, for histologic diagnosis.	Examination pending.	221—Blood, for Widal's reaction.	Positive.
197—Tumor from tongue and epiglottis, for histologic diagnosis.	Round-cell sarcoma.	222—Fluid from pleural cavity, to determine if tubercle bacilli be present.	Negative.*
198—Fluid from pleural cavity, to determine character of infection.	No bacteria found.	223—Growth from cervix, for histologic diagnosis.	Examination pending.
199—Glands removed from axilla; histologic diagnosis.	Tuberculosis.	224—Amputated right leg; histologic diagnosis.	Osteosarcoma of lower end of femur.
200—Elephantiasis of scrotum; histologic diagnosis.	Elephantiasis.	225—Culture tube inoculation, to determine character of infection.	Micrococcus pyogenes aureus.
201—Part of lower jaw, for histologic diagnosis.	Epithelioma with associated pyogenic infection.	226—Shreds of tissue, for histologic diagnosis.	Endometritis.
202—Culture tube inoculation, to determine character of infection.	Mixed infection. Micrococcus pyogenes aureus, and Micrococcus pyogenes albus.	227—Sputum, for tubercle bacilli.	Not present.
203—Culture tube inoculation; to determine character of infection.	No growth.	228—Sputum, for tubercle bacilli.	Not present.
204—Culture tube inoculation, to determine character of infection.	Micrococcus pyogenes albus.	229—Intestine and attached mesentery, for histologic diagnosis.	Carcinomatosis of peritoneum.
205—Testicle, for histologic diagnosis.	Alveolar sarcoma showing slight melanosis.	230—Blood, for Widal's reaction.	Negative.*
206—Culture tube inoculation, to determine character of infection.	Micrococcus pyogenes albus.	231—Culture tube inoculation, to determine character of infection.	No bacteria found.
207—Glands from axilla and neck, for histologic diagnosis.	Tuberculosis.	232—Blood examination.	Symptomatic anemia.
208—Culture tube inoculation, to determine character of infection.	Micrococcus pyogenes albus.	233—Tissue from thumb, for histologic diagnosis.	Mixed-cell sarcoma (giant and spindle cell).
209—Culture tube inoculation, to determine character of infection.	Streptococcus pyogenes.	234—Blood examination.	Symptomatic anemia.
210—Culture tube inoculation, to determine character of infection.	Bacillus of Weeks.	235—Urine.	Negative.*
211—Sputum, for tubercle bacilli.	Not present.	236—Culture tube inoculation, to determine character of infection.	Bacillus diphtheriae.
212—Urine, for tubercle bacilli.	Not present.	237—Culture tube inoculations, to determine character of infection.	Micrococcus pyogenes albus.
213—Tumor from face, for histologic diagnosis.	Sarcoma.	238—Culture tube inoculation, to determine character of infection.	Micrococcus (staphylococcus) pyogenes albus.
214—Uterus and appendages.	Papillary cancer.	239—Blood, for Widal's reaction.	Negative.*
215—Culture tube inoculations, to determine character of infection.	Diplococcus pneumoniae.	240—Blood, for Widal's reaction.	Negative.*
216—Blood, for Widal's reaction.	Negative.*	241—Blood examination.	Negative.*
217—Sputum, for tubercle bacilli.	Not present.	242—Piece of rectum and sacrum, for histologic diagnosis.	Adenoma.
		243—Culture tube inoculation, to determine character of infection.	No growth.
		244—Culture tube inoculation, to determine character of infection.	Bacillus typhosus.
		245—Tissue from necrosed ribs, for histologic diagnosis.	Inflammatory tissue.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
246—Tissue washed from stomach (?; histologic diagnosis.	Fibrinous pseudomembrane.	270—Culture tube inoculation, to determine character of infection.	No bacteria found.
247—Ascitic fluid from abdominal cavity, to determine character of infection.	Sterile.	271—Sputum, for tubercle bacilli.	Present.
248—Sputum, for tubercle bacilli.	Present.	272—Glans penis, for histologic diagnosis.	Syphilitic ulceration, (tertiary).
249—Sputum, for tubercle bacilli.	Not present.	273—Urine.	Negative.*
250—Urine, for tubercle bacilli.	Not present.	274—Culture tube inoculations, to determine character of infection.	Bacillus coli communis.
251—Culture tube inoculation, to determine character of infection.	Bacillus pyogenes foetidus.	275—Piece of tongue, for histologic diagnosis.	Squamous-cell epithelioma.
252—Culture tube inoculations, to determine character of infection.	Micrococcus (staphylococcus) pyogenes albus.	276—Culture tube inoculation, to determine character of infection.	Mixed infection. Streptococcus pyogenes, and white yeast.
253—Culture tube inoculation, to determine character of infection.	Mixed infection Micrococcus (staphylococcus) pyogenes aureus and Bacillus pyogenes foetidus.	277—Sputum, for tubercle bacilli.	Present.
254—Two microscope slides for diagnosis; section of mamma.	Adenofibroma.	278—Growth from cervix, for histologic diagnosis.	Inflammatory tissue.
255—Fragments of bone, for histologic diagnosis.	Osteitis with slight periostitis.	279—Urine.	Negative.*
256—Tumor from knee, for histologic diagnosis.	Tuberculosis.	280—Culture tube inoculations, to determine character of infection.	Staphylococcus aureus.
257—Gauze, for bacteriologic diagnosis.	Bacillus pyocyaneus.	281—Culture tube inoculation, to determine character of infection.	Streptococcus pyogenes.
258—Tumor, for histologic diagnosis.	Mass of unstriated muscle tissue.	282—Culture tube inoculation and smear preparations, to determine character of infection.	Micrococcus (staphylococcus) pyogenes aureus.
259—Sputum, for tubercle bacilli.	Not present.	283—Blood, for Widal's reaction.	Positive.
260—Culture tube inoculation, to determine character of infection.	Diplococcus pneumoniae.	284—Testicle, for histologic diagnosis.	Tuberculosis.
261—Sputum, for tubercle bacilli.	Present.	285—Sputum, for tubercle bacilli.	Not present.
262—Urine.	Pyuria.	286—Milk, to determine character of infection.	Sterile.
263—Growth from lip, for histologic diagnosis.	Squamous-cell epithelioma.	287—Tissue from leg, for histologic diagnosis.	From specimen submitted, no satisfactory report can be given.
264—Culture tube inoculations, to determine character of infection.	Diplococcus pneumoniae.	288—Sputum, for tubercle bacilli.	Not present.
265—Culture tube inoculations, to determine character of infection.	Diplococcus pneumoniae.	289—Fluid from lumbar puncture, to determine character of infection.	Sterile.
266—Culture tube inoculations, to determine character of infection.	Bacillus saprogenes.	290—Blood examination.	Symptomatic anemia.
267—Culture tube inoculations and smear preparations, to determine character of infection.	Diplococci and micrococci, not plated into pure cultures.	291—Sputum, for tubercle bacilli.	Present.
268—Sputum, for tubercle bacilli.	Not present.	292—Tumor from neck, for histologic diagnosis.	Report pending.
269—Piece of tongue, for histologic diagnosis.	Positive diagnosis not possible from material submitted.	293—Urine.	Hematuria.
		294—Sputum, for tubercle bacilli.	Present.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
295—Blood examination.	Negative.*	320—Culture tube inoculation, to determine character of in- fection.	Micrococcus pyogenes albus.
296—Blood, for Widal's reaction.	Negative.*	323—Urine.	Chronic interstitial nephritis.
297—Tumor of breast, for histo- logic diagnosis.	Scirrhus carcinoma.	324—Nerve, for histologic diag- nosis.	Negative.*
298—Sputum, for tubercle bacilli.	Not present.	325—Tissue removed from palm of hand; histologic diag- nosis.	Inflammatory tissue.
299—Sputum, for tubercle bacilli.	Present.	326—Urine.	Renal hematuria.
300—Uterus, for histologic diag- nosis.	Leiomyoma.	327—Urine.	Negative.*
301—Urine.	Negative.*	328—Right sterno-mastoid muscle, for histologic diagnosis.	Negative.*
302—Tumor from tongue, for his- tologic diagnosis.	Papilloma.	329—Left sterno-mastoid muscle, for histologic diagnosis.	Negative.*
303—Culture tube inoculations, to determine if ray fungus be present.	Not present.	330—Culture tube inoculations, to determine character of in- fection.	Bacillus coli communis.
304—Nerve, for histologic diag- nosis.	Negative.*	331—(a) Scrapings from arm, for histologic diagnosis, (b) in- oculation from same, to de- termine character of in- fection.	(a) Tuberculosis. (b) Staphylococcus pyogenes aureus.
305—Culture tube inoculation, to determine character of in- fection.	Diplococcus pneumoniae.	332—Part of breast and axillary glands, for histologic diag- nosis.	Cystic fibro-adenoma.
306—Part of inferior maxilla, con- taining 6 teeth; histologic diagnosis	Examination in progress.	333—Urine.	Parenchymatous nephritis.
307—Tissue from mouth and tongue, for histologic diag- nosis.	Examination in progress.	334—Urine.	Negative.*
308—Blood, for Widal's reaction	Negative.*	335—Urine.	Hematuria.
309—Sputum, for tubercle bacilli.	Not present.	336—Tissue from upper jaw, for histologic diagnosis.	Squamous-cell epithelioma.
310—Mass removed from cheek; pathologic diagnosis.	Squamous-cell epithelioma.	337—Kidney, for histologic diag- nosis.	Alveolar sarcoma.
311—Tissue from ileo-caecal re- gion; histologic diagnosis.	Inflammatory tissue.	338—Urine.	Negative.*
312—Tissue curetted from uterus, for histologic diagnosis.	Piece of attached placenta.	339—Tumor of breast, for histo- logic diagnosis.	Scirrhus carcinoma.
313—Blood examination.	Pernicious anæmia (?)	340—Tumor of axilla, for histo- logic diagnosis.	Round-cell sarcoma.
314—Urine.	Cystitis.	341—Blood examination.	Symptomatic anæmia.
315—Ulcer removed from fore- head.	Tubulated epithelioma.	342—Stool, to determine if tuber- cle bacilli be present.	Present.
316—Nerves, for histologic diag- nosis.	Negative.*	343—Tissue removed from over sacrum; histologic diag- nosis.	Squamous-cell epithelioma.
317—Tumor of superior max- illa (?).	Papilloma.	344—Urine.	Hematuria.
318—Culture tube inoculations, to determine character of in- fection.	Diplobacillus infection.	345—Blood examination.	Symptomatic anæmia.
319—Urine.	Chronic interstitial nephritis.	346—Growth from peritoneum, for histologic diagnosis.	Specimen lost.
320—Urine.	Chronic interstitial nephritis.	347—Blood examination.	Negative.*
321—Urine.	Chronic interstitial nephritis.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
348—Sputum, for tubercle bacilli.	Not present.	377—Culture tube inoculations, to determine character of in- fection.	No bacteria found.
349—Tissue removed from axilla; histologic diagnosis.	Alveolar lymphosarcoma.	378—Skin from over knee joint, for histologic diagnosis.	Tuberculosis (Lupus).
350—Tumor of breast, for histo- logic diagnosis.	Report pending.	379—Left breast, for histologic diagnosis.	Scirrhus carcinoma.
351—Glands from neck, for histo- logic diagnosis.	Tubercular adenitis.	380—Blood, for malaria organisms	Not present.
352—Tissue from cheek, for histo- logic diagnosis.	Squamous-cell epithelioma.	381—Blood, for malaria organisms	Not present.
353—Coccyx, for histologic diag- nosis.	Normal.	382—Blood, for malaria organisms	Not present.
354—Urine.	Spermatorrhœa.	383—Blood, for malaria organisms	Not present.
355—Blood, for malaria organisms	Not present.	384—Blood, for malaria organisms	Not present.
356—Blood, for malaria organisms	Not present.	385—Blood, for malaria organisms	Not present.
357—Blood, for malaria organisms	Not present.	386—Blood, for malaria organisms	Present.
358—Blood, for malaria organisms	Not present.	387—Blood, for malaria organisms	Not present.
359—Blood, for malaria organisms	Not present.	388—Blood, for malaria organisms	Not present.
360—Blood, for malaria organisms	Not present.	389—Blood, for malaria organisms	Not present.
361—Blood, for malaria organisms	Not present.	390—Blood, for malaria organisms	Not present.
362—Blood, for malaria organisms	Not present.	391—Blood, for malaria organisms	Present.
363—(a) Blood, for malaria or- ganisms. (b) Pus from hand, to determine character of infection.	(a) Not present. (b) Staphylococcus pyogenes aureus.	392—Blood, for malaria organisms	Not present.
364—Blood, for Widal's reaction	Positive.	393—Sputum, for tubercle bacilli.	Not present.
365—Blood, for Widal's reaction.	Positive.	394—Stool, for amoebæ.	Not present.
366—Blood, for Widal's reaction.	Positive.	395—Gauze from uterus and va- gina, to determine character of infection.	Streptococci and staphylococci.
367—Blood, for Widal's reaction.	Positive.	396—Urine.	Cystitis.
368—Blood, for Widal's reaction.	Positive.	397—Right breast, for histologic diagnosis.	Report pending.
369—Growth from right inguinal region, for histologic diag- nosis.	Mixed-cell sarcoma.	398—Blood, for malaria organisms	Not present.
370—Sputum, for tubercle bacilli.	Present.	399—Blood, for malaria organisms	Present.
371—Urine, for tubercle bacilli.	Present.	400—Blood, for malaria organisms	Not present.
372—Blood, for malaria organisms	Not present.	401—Blood, for malaria organisms	Present.
373—Blood, for malaria organisms	Not present.	402—Blood, for malaria organisms	Hyaline and pigmented forms present.
374—Blood, for malaria organisms	Not present.	403—Blood, for Widal's reaction.	Negative.*
375—Blood, for malaria organisms	Not present.	404—Blood, (a) for Widal's reaction; (b) for malaria organisms.	(a) Negative.* (b) Present.
376—Blood, for malaria organisms	Not present.	405—Blood, (a) for Widal's reaction; (b) for malaria organisms.	(a) Negative.* (b) Present.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
406—Blood, (a) for Widal's reaction; (b) for malaria organisms.	(a) Negative.* (b) Not present.	434—Breast, for histologic diag- nosis.	Carcinoma (encephaloid).
407—Blood, (a) for Widal's reaction; (b) for malaria organisms.	(a) Negative.* (b) Not present.	435—Urine.	Negative.*
408—Blood examination.	Chlorosis.	436—Blood, for malaria organisms	Not present.
409—Blood, for malaria organisms	Not present.	437—Blood, for malaria organisms	Not present.
410—Blood, for malaria organisms	Not present.	438—Blood, for malaria organisms	Not present.
411—Blood, for Widal's reaction.	Negative.*	439—Blood, for malaria organisms	Not present.
412—Blood, for malaria organisms	Not present.	440—Blood, for malaria organisms	Not present.
413—Blood, for malaria organisms	Present.	441—Blood, for malaria organisms	Not present.
414—Blood, for malaria organisms	Not present.	442—Blood, for malaria organisms	Not present.
415—Blood, for malaria organisms	Not present.	443—Blood, for malaria organisms	Not present.
416—Blood, for malaria organisms	Negative.*	444—Blood, for malaria organisms	Not present.
417—Blood, for malaria organisms	Present.	445—Blood, for malaria organisms	Not present.
418—Spreads from ankle joint, to determine if gonococci be present.	Present.	446—Blood, for malaria organisms	Not present.
419—Blood, for Widal's reaction.	Positive.	447—(a) Sputum, for tubercle bac- illi; (b) Urine, for tubercle bacilli.	(a) Present. (b) Not present.
420—Blood, for Widal's reaction.	Positive.	448—Culture tube inoculation, to determine character of in- fection.	Mixed infection. Staphylococcus pyogenes albus and Bacillus pyocyaneus.
421—Blood, for Widal's reaction.	Positive.	449—Culture tube inoculation, to determine character of in- fection.	No bacteria found.
422—(a) Urine, (b) Blood, for malaria organisms.	(a) Negative.* (b) Present.	450—Culture tube inoculation, to determine character of in- fection.	No bacteria found.
423—Blood, (a) for malaria organisms; (b) for Widal's reaction.	(a) Not present. (b) Positive.	451—Uterus, for histologic diag- nosis.	Carcinoma (squamous).
424—Blood, (a) for Widal's reaction; (b) for malaria organisms.	(a) Positive. (b) Not present.	452—Right submaxillary gland, for histologic diagnosis.	Normal.
425—Sputum, for tubercle bacilli.	Not present.	453—Tonsil, for histologic diag- nosis.	Round-cell sarcoma.
426—Sputum, for tubercle bacilli.	Not present.	454—Sputum, for tubercle bacilli.	Not present.
427—Blood examination.	Chlorosis (?).	455—Sputum, for tubercle bacilli.	Not present.
428—Blood examination.	Symptomatic anemia.	456—Left testicle, for histologic diagnosis.	Report pending.
429—Tumor from rectum, for his- tologic diagnosis.	Scirrhus carcinoma.	457—Blood examination.	Negative.*
430—Tumor from cheek, for his- tologic diagnosis.	Squamous epithelioma.	458—Blood examination.	Negative.*
431—Sputum, for tubercle bacilli.	Not present.	459—Culture tube inoculation, to determine character of in- fection.	Bacillus pyocyaneus.
432—Breast, for histologic diag- nosis.	Scirrhus carcinoma.	460—Sputum, for tubercle bacilli.	Not present.
433—Sputum, for tubercle bacilli.	Present.	461—Sputum, for tubercle bacilli.	Not present.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
462—Blood examination.	Negative.*	488—Blood, for Widal's reaction.	Negative.*
463—Breast, for histologic diagnosis.	Carcinoma.	489—Blood, for malaria organisms	Present.
464—Nerve from popliteal space, for histologic diagnosis.	Report pending.	490—Culture tube inoculation, to determine character of infection.	Staphylococcus pyogenes aureus.
465—Tissue from elbow joint, for histologic diagnosis.	Inflammatory tissue.	491—Culture tube inoculations, to determine character of infection.	Mixed infection. Bacillus pyocyaneus and Bacillus subtilis.
466—Amputated leg and part of thigh, for histologic diagnosis.	Gangrene	492—Sputum, for tubercle bacilli.	Present.
467—Culture tube inoculations, to determine character of infection.	Mixed infection. Bacillus coli communis, and staphylococcus albus.	493—Blood examination.	Negative.*
468—Ovaries, for histologic diagnosis.	General carcinomatosis.	494—(a) Sputum, for tubercle bacilli; (b) blood examination.	(a) Not present. (b) Negative.*
469—Discharge from abscess, for tubercle bacilli.	Not present.	495—Blood, (a) for malaria organism; (b) general examination.	(a) Present. (b) Negative.*
470—Urine.	Hematuria.	496—Piece of frontal bone, for histologic diagnosis.	Negative.*
471—(a) Blood, for Widal's reaction; (b) Urine, for diazzo reaction.	(a) Positive. (b) Positive.	497—Tumor from lower jaw (?), for histologic diagnosis.	Carcinoma (squamous).
472—Sputum, for tubercle bacilli	Not present.	498—Testicle, for histologic diagnosis.	Normal testicle and vas deferens.
473—Uterus, for histologic diagnosis.	Carcinoma, cylindric-cell.	499—Discharge from axillary abscess, for bacteriologic diagnosis.	Staphylococci present, no tubercle bacilli.
474—Tissue from floor of mouth, for histologic diagnosis.	Epithelioma.	500—Tumor from face, for histologic diagnosis.	Carcinoma (squamous).
475—Fluid aspirated from pleural cavity, to determine character of infection.	Staphylococci.	501—Sputum, for tubercle bacilli.	Present.
476—Urine, for tubercle bacilli.	Not present.	502—Sputum, for tubercle bacilli.	Not present.
477—Culture tube inoculation, to determine character of infection.	Staphylococcus pyogenes albus.	503—Sputum, for tubercle bacilli.	Not present.
478—Sputum, for tubercle bacilli.	Present.	504—Fluid from pleural cavity, for bacteriologic diagnosis.	Negative.*
479—Blood, for streptococci.	Not present.	505—Secretion from eye, to determine character of infection.	Negative.*
480—Tumor of breast, for histologic diagnosis.	Intracanalicular fibroma.	506—Sputum, for tubercle bacilli.	Not present.
481—Urine.	Chronic interstitial nephritis.	507—Tumor of left pectoral region, for histologic diagnosis.	Angioma hypertrophicum.
482—Sputum, for tubercle bacilli.	Not present.	508—Urine.	Glycosuria; albuminuria.
483—Culture tube inoculation, to determine character of infection.	Bacillus pyocyaneus.	509—Urine.	Glycosuria.
484—Blood, for malaria organisms	Not present.	510—Sputum, for tubercle bacilli.	Not present.
485—Blood, for streptococci.	Not present.	511—Blood, (a) for malaria organism; (b) general examination.	(a) Present. (b) Symptomatic anemia.
486—Culture tube inoculations, to determine character of infection.	Staphylococcus pyogenes albus.	512—Urine, for lead.	Not present.
487—Tumor from right side of neck, for histologic diagnosis.	Spindle-cell sarcoma.	513—Sputum, for tubercle bacilli.	Present.
		514—Scrapings from visceral layer of pleura, for histologic diagnosis.	Endothelioma.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
515—Culture tube inoculations, to determine character of infection.	No growth.	540—Fluid from abdominal cavity, to determine character of infection.	No bacteria present.
516—Milk, to determine character of infection.	Sterile.	541—Tumor of mammary gland, for histologic diagnosis.	Scirrhus carcinoma.
517—Culture tube inoculations, to determine character of infection.	Bacillus coli communis.	542—Sputum, for tubercle bacilli.	Not present.
518—Gastric contents, for hydrochloric acid.	Present.	543—Sputum, for tubercle bacilli.	Present.
519—Left testicle, for histologic diagnosis.	Cystic disease of testicle with secondary pyogenic infection.	544—Specimen from spinal cord, following fracture of the vertebrae; removed post-mortem.	Septic meningitis. Extensive softening of the cord, with tract degeneration.
520—Growth from finger, for histologic diagnosis.	Squamous-cell epithelioma.	545—Inoculations from tissues in Case No. 547, to determine character of infection.	Mixed infection. Bacillus pyocyaneus, micrococcus pyogenes albus, and bacillus pyogenes foetidus.
521—Membrane from cheek, for histologic diagnosis.	Inflammatory tissue.	546—Blood examination.	Negative.*
522—Gastric contents, for hydrochloric acid.	Present.	547—Blood examination.	Slight lymphocytosis.
523—Growth from neck, for histologic diagnosis.	Tuberculous lymphadenitis	548—Sputum, for tubercle bacilli.	Not present.
524—Curettings from interior of uterus, for histologic diagnosis.	Acute infection of endometrium.	549—Lymphatic glands from neck, for histologic diagnosis.	Tuberculosis lymphadenitis.
525—Fluid obtained by lumbar puncture, for bacteriologic diagnosis.	No bacteria found.	550—Ovaries, uterus, and lining membrane of pelvis abscess, for histologic diagnosis.	Tissue shows evidence of chronic, subacute and acute inflammation, and contains numerous staphylococci.
526—Gastric contents, for hydrochloric and lactic acids.	Both acids present.	551—Inoculation from abscess, to determine character of infection.	Pure culture of staphylococcus pyogenes aureus.
527—Blood, for Widal's reaction.	Negative *	552—Sputum, for tubercle bacilli.	Negative.*
528—Blood examination.	Symptomatic anemia.	553—Inoculation from ankle joint, to determine character of infection.	Pure culture of staphylococcus pyogenes albus.
529—Blood examination.	Contains hematozoön malariae (aestivo-autumnal form).	554—Wall of inflamed prepatella bursa, to determine character of infection.	Staphylococcus pyogenes albus, obtained in pure culture.
530—Inoculation from post-thyroid abscess, to determine character of infection.	Pure cultures of the staphylococcus pyogenes aureus.	555—Amputated leg, extensive ulcerative processes, involving ankle joint and tarsal articulation.	Report pending.
531—Inoculation from middle ear, to determine character of infection.	Pure culture of the bacillus pyogenes foetidus.	556—Membranous sac with contained polypoid tumor, removed from inguinal region, for histologic diagnosis.	Report pending.
532—Sputum, to determine if tubercle bacilli be present.	Not present.	557—Sputum, for tubercle bacilli.	Not present.
533—Inoculation from cyst of thyroid, to determine character of infection.	No growth.	558—Blood examination.	Slight symptomatic anemia.
534—Blood examination.	Negative.*	559—Sputum, for tubercle bacilli.	Not present.
535—Sputum, for tubercle bacilli.	Not present.	560—Blood examination.	Negative.*
536—Fluid from pleural cavity, to determine character of infection.	No bacteria found.	561—Blood, for Widal's reaction.	Negative.*
537—Blood examination.	Inflammatory leucocytosis.	562—Blood, for Widal's reaction.	Positive.
538—Inoculations from ulcer of cheek, to determine character of infection.	Pure growth of staphylococcus pyogenes albus.		
539—Sputum, for tubercle bacilli.	Present.		

The following is a list of specimens and materials examined in the Laboratories during the year 1899 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
566—Sputum, for tubercle bacilli.	Negative.*	590—Urine.	Albuminuria with casts.
567—Breast, for histologic diagnosis.	Material unfit for examination.	591—Tumor from neck, for histologic diagnosis.	Mixed cell sarcoma.
568—Sputum, for tubercle bacilli.	Negative.*	592—Tumor from neck, for histologic diagnosis.	Mixed cell sarcoma.
569—Tumor from right eye, for histologic diagnosis.	No report submitted.	593—Gastric contents, submitted for examination as to coloring matter.	Contains bile.
570—Gastric contents, for hydrochloric acid.	No hydrochloric acid present.	594—Blood examination.	Chlorotic anemia.
571—Tissue from breast, for histologic diagnosis.	No report submitted.	595—Urine.	Negative.*
572—Leg, for histologic diagnosis.	Tuberculosis.	596—Gastric contents, for hydrochloric and lactic acids.	Neither present.
573—Inoculation from throat, to determine character of infection.	Staphylococcus pyogenes aureus.	597—Material from postmortem, to determine cause of death.	Biliary stricture.
574—Specimen from abortion, for histologic diagnosis.	Placental infarction.	598—Tumor from breast, for histologic diagnosis.	Acinous adenoma.
575—Calculus.	No report requested.	599—Sputum, for tubercle bacilli.	Negative.*
576—Gauze dressings, for bacteriologic examination.	Mixed infection. Bacillus pyocyaneus, and bacillus coli communis.	600—Fallopian tube and ovary, for histologic diagnosis.	Chronic fibroid, and acute septic, ovariitis.
577—Bony tumor from leg, for histologic diagnosis.	Myxofibroma undergoing probable sarcomatous change.	601—Vaginal discharge, for bacteriologic examination.	Mixed infection. Micrococcus pyogenes aureus, bacillus pyogenes foetidus, and bacillus pyocyaneus
578—Blood examination.	Polycythemia.	602—Blood examination.	Chlorosis.
579—Breast, for histologic examination.	No report requested.	603—Serum aspirated from knee, for bacteriologic examination.	Staphylococcus pyogenes aureus.
580—Inoculation from tonsil, to determine character of infection.	Diplococcus of pneumonia.	604—Right lobe of thyroid gland, for histologic diagnosis.	Encephaloid cancer.
581—Urine.	Albuminuria.	605—Gastric contents, for (a) hydrochloric acid. (b) lactic acid.	(a) Negative.* (b) Positive.
582—Blood, for Widal's reaction.	Positive.	606—(a) Sputum, for tubercle bacilli. (b) Stool, for tubercle bacilli.	(a) Present. (b) Present.
583—Sputum, for tubercle bacilli.	Negative.*	607—Sputum, for tubercle bacilli.	Negative.*
584—Breast and axillary glands, for histologic diagnosis.	Encephaloid carcinoma.	608—Inoculation from ear, to determine character of infection.	Proteus sulfueus (Lindenborn).
585—Tissue from brain, for histologic diagnosis.	Specimen lost.	609—Inoculation from ears, to determine character of infection.	Pure cultures of staphylococcus pyogenes aureus.
586—Gastric contents, for hydrochloric and lactic acids.	Contains lactic acid.	610—Urine.	Albuminuria with casts.
587—Inoculation from wound, to determine character of infection.	Staphylococcus pyogenes aureus.	611—Nerve, for histologic diagnosis.	Specimen destroyed.
588—Inoculation from granulation tissue, to determine character of infection.	Staphylococcus pyogenes aureus.	612—Head of tibia, for histologic diagnosis.	Mixed cell sarcoma.
589—Lungs from postmortem, for histologic diagnosis.	Emphysema.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
613—Breast and pectoral muscles, for histologic diagnosis.	Pericanalicular fibroma, scirrhous carcinoma.	643—Urine.	Negative.*
614—Urine.	Negative.*	644—Urine.	Negative.*
615—Blood, for Widal's reaction.	Negative.*	645—Tumor from breast, for his- tologic diagnosis.	Scirrhous carcinoma.
616—Inoculation from appendix, to determine character of infection.	No growth.	646—Pus from lachrymal duct, for bacteriologic examination.	Diplococcus of Sternberg.
617—Blood, for malaria organisms	Not present.	647—Spreads made from secretion from conjunctiva, for bac- teriologic examination.	Staphylococci, kind not determined.
618—Blood examination.	Simple anemia.	648—Blood, for Widal's reaction.	Positive.
619—Blood examination.	Simple anemia.	649—Inoculation from leg, to de- termine character of infec- tion.	Staphylococcus pyogenes albus.
620—Inoculation from eye, to determine character of in- fection.	No growth.	650—Sputum, for tubercle bacilli.	Present.
621—Inoculation from eye, to determine character of in- fection.	Negative.*	651—Urine, for tubercle bacilli.	Present.
622—Breast, for histologic diag- nosis.	Scirrhous carcinoma.	652—Glands from submaxillary region, for histologic diag- nosis.	Tuberculous lymphadenitis.
623—Gastric contents.	Hematemesis.	653—Inoculation from conjunctiva, to determine character of infection.	Diplococcus of Sternberg.
624—Material from postmortem, for histologic diagnosis.	Marasmus (provisioned).	654—Superior maxilla, for histo- logic diagnosis.	Specimen lost.
625—Serum from side, for bacteri- ologic examination.	Bacillus subtilis.	655—Tissue from eye, for his- tologic diagnosis.	Tubulated epithelioma.
626—Left breast, for histologic diagnosis.	Pericanalicular fibroma.	656—Spreads from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.
627—Blood examination.	Negative.*	657—Sputum, for tubercle bacilli.	Negative.*
628—Blood examination.	Negative.*	658—Tumor from left breast, for histologic diagnosis.	Fibroadenoma.
629—Sputum, for tubercle bacilli.	Negative.*	659—Blood examination.	Negative.*
630—Urine.	Negative.*	660—Spreads from conjunctiva, for bacteriologic examina- tion.	Diplobacillary infection.
631—Specimens from postmortem.	Specimens lost.	661—Inoculation from abscess of right side, to determine character of infection.	Sterile.
632—Sputum, for tubercle bacilli.	Negative.*	662—Tissue from neck, for his- tologic diagnosis.	Suppurative inflammation.
633—Inoculation from appendix, to determine character of in- fection.	Sterile.	663—Inoculation from appendix, to determine character of infection.	Sterile.
634—Discharge from cheek, for bacteriologic examination.	Staphylococcus pyogenes albus.	664—Glands from neck, for his- tologic diagnosis.	Tuberculous lymphadenitis.
635—Sputum, for tubercle bacilli.	Negative *	665—Silver foil, to determine if infected.	Sterile.
636—Fluid from side, for bacteri- ologic examination.	Inflammatory exudate.	666—Inoculation from green soap, to determine if infected.	Sterile.
637—Tissue taken from face, for histologic diagnosis.	Tubulated epithelioma.	667—Fluid aspirated from knee, for bacteriologic examina- tion.	Sterile.
638—Inoculation from cystic tu- mor from neck, to determine character of infection.	Staphylococcus pyogenes aureus.	668—Spreads from conjunctiva, for bacteriologic examina- tion.	Mixed infection. Di- plococcus of Stern- berg, diplococcus of Axenfeld and Peters.
639—Cystic tumor from neck, for histologic diagnosis.	Suppurating cystoma.	669—Fluid from knee, for bac- teriologic examination.	Sterile.
640—Secretion from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.		
641—Appendix, for histologic di- agnosis.	Suppurative appendicitis.		
642—Piece of cervix, for histologic diagnosis.	Adeno-carcinoma.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
670—Sputum, for tubercle bacilli.	Negative.*	698—Urine.	Hematuria.
671—Inoculation from appendix, to determine character of in- fection.	Bacillus coli communis.	699—Urine.	Hematuria.
672—Discharge from uterus, for bacteriologic examination.	Blood clot.	700—Fluid drawn from side, for bacteriologic examination.	Pleuritis due to diplo- coccus of Sternberg.
673—Urine.	Negative.*	701—Spreads from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.
674—Blood examination.	Negative.*	702—Inoculation from ovary, to determine character of in- fection.	Staphylococcus pyogenes albus.
675—Breast, for histologic diag- nosis.	Mixed-cell pericana- llular, and intraca- nalicular sarcoma.	703—Oviduct and ovary, for his- tologic diagnosis.	Simple dermoid cyst of ovary.
676—Urine.	Negative.*	704—Sputum, for tubercle bacilli.	Negative.*
677—Urine.	Albuminuria.	705—Sputum, for tubercle bacilli.	Negative.*
678—Urine.	Albuminuria.	706—Sputum, for tubercle bacilli.	Present.
679—Ovary, for histologic diag- nosis.	Acute interstitial oöphoritis.	707—Urine.	Albuminuria.
680—Breast and axillary gland, for histologic diagnosis.	Scirrhus carcinoma of mammary gland with secondary in- volvement of axil- lary lymphatics.	708—Sputum, for tubercle bacilli.	Negative.*
681—Left axillary gland, for his- tologic diagnosis.	Tuberculous lymphadenitis.	709—Tissue from inside of trachea, for histologic diagnosis.	Specimen lost.
682—Kidney, adrenal, and fat, for histologic diagnosis.	Congenital cyst of kidney.	710—Sputum, for tubercle bacilli.	Negative.*
683—Urine.	Negative.*	711—Sputum, for tubercle bacilli.	Negative.*
684—Secretion from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.	712—Sputum, for tubercle bacilli.	Negative.*
685—Urine.	Negative.*	713—Thoracic viscera, for his- tologic diagnosis.	Aneurism of arch of aorta.
686—Blood, for Widal's reaction.	Positive.	714—(a) Blood examination. (b) Gastric contents.	(a) Symptomatic anemia. (b) Oppeler-Boas bacillus.
687—Blood examination.	Simple anemia.	715—Urine.	Material not suitable for examination.
688—Ovarian tumor, for histo- logic diagnosis.	Multilocular prolifer- ous papillary cyst- adenoma.	716—Spreads from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.
689—Blood examination.	Negative.*	717—Sputum, for tubercle bacilli.	Negative.*
690—Secretion from conjunctiva, for bacteriologic examina- tion.	Gonococcus.	718—Nerve from arm, for his- tologic diagnosis.	Material unfit for examination.
691—Growth from cheek, for his- tologic diagnosis.	Squamous cell epithelioma.	719—Blood examination.	Pernicious anemia.
692—Inoculation from throat, to determine character of in- fection.	Diphtheria.	720—Spreads from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.
693—Spreads from conjunctiva, for bacteriologic examina- tion.	No bacteria demonstrable.	721—Blood, for malaria organ- isms.	Negative.*
694—Urine.	Pyuria.	722—Right lobe of thyroid gland, for histologic diagnosis.	Hyperplastic goitre.
695—Spreads and inoculation from conjunctiva, to deter- mine character of infection.	No bacteria demonstrable.	723—Calculus, for histologic ex- amination.	Uric acid.
696—Spreads from conjunctiva, for bacteriologic examina- tion.	No bacteria demonstrable.	724—Tissue from ulcer of foot, for histologic examination.	Specimen lost.
697—Sputum, for tubercle bacilli.	Negative.*	725—Spreads from conjunctiva, for bacteriologic examina- tion.	Diplococcus of Sternberg.
		726—Spreads from conjunctiva, for bacteriologic examina- tion.	No bacteria demonstrable.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
727—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.	754—Spreads from conjunctiva, for bacteriologic examination	No bacteria demonstrable.
728—Inoculation from appendix, to determine character of infection.	Staphylococcus pyogenes aureus.	755—Tissue from uterus, for histologic diagnosis	Specimen unfit for examination.
729—Inoculation from mammary cyst to determine character of infection.	Staphylococcus pyogenes albus.	756—Left ovary and oviduct, for histologic diagnosis.	Ovarian tuberculosis and tuberculosis of Fallopian tube.
730—Urine.	Albuminuria with casts.	757—Right ovary, for histologic diagnosis.	Ovarian abscess.
731—Tumor from left temporal region, for histologic diagnosis.	Ulcerating squamous-cell epithelioma.	758—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.
732—Urine.	Negative.*	759—Spreads from conjunctiva, for bacteriologic examination.	No bacteria demonstrable.
733—Inoculation from appendix, to determine character of infection.	Staphylococcus pyogenes albus.	760—Sputum, for tubercle bacilli.	Present.
734—Inoculation from hip-joint abscess, for tubercle bacilli, also typhoid bacilli.	Not demonstrable.	761—Sputum, for tubercle bacilli.	Negative.*
735—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.	762—Tumor and enlarged glands, for histologic diagnosis.	Melanotic sarcoma.
736—Spreads from right eye, for bacteriologic examination.	Diplococcus of Sternberg.	763—Blood examination.	Negative.*
737—Sputum, for tubercle bacilli.	Negative.*	764—Inoculation from abscess, to determine character of infection.	Material unfit for examination.
738—Urine.	Negative.*	765—Tissue from breast and glands, for histologic diagnosis.	Encephaloid cancer.
739—Urine.	Negative.*	766—Urine.	Pyuria.
740—Urine.	Negative.*	767—Polyp of uterus, for histologic diagnosis.	Adenoma papilliferum.
741—Tumor from forearm, for histologic diagnosis.	Material unfit for examination.	768—Spreads from corneal ulcer, for bacteriologic examination.	No bacteria demonstrable.
742—Urine.	Albuminuria with casts.	769—Urine.	Negative.*
743—Blood examination.	Pernicious anemia.	770—Blood examination.	Simple anemia.
744—Tissue from rectum, for histologic diagnosis.	Scirrhus carcinoma.	771—Tumor from right tonsil, for histologic examination.	Endothelioma.
745—Mass from mouth, for histologic diagnosis.	Encephaloid carcinoma.	772—Brain and spinal cord, for histologic diagnosis.	Tuberculous meningitis.
746—Gastric contents, for hydrochloric and lactic acids.	Present.	773—Blood, for malaria organisms.	Negative.*
747—Urine.	Albuminuria.	774—Sputum, for tubercle bacilli.	Negative.*
748—Sputum, for tubercle bacilli.	Negative.*	775—Spreads from eye, for bacteriologic examination.	Diplococcus of Sternberg.
749—Sputum, for tubercle bacilli.	Negative.*	776—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.
750—Left lobe of liver, for histologic diagnosis.	Carcinoma of liver.	777—Spreads from membrane of mouth, for bacteriologic examination.	Diplococcus of Sternberg.
751—Blood examination.	Anemia (Symptomatic).	778—Cyst from liver, for histologic diagnosis.	Echinococcus cyst.
752—Spreads from conjunctiva, for bacteriologic examination.	Negative.*	779—Sputum, for tubercle bacilli.	Negative.*
753—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.	780—Blood examination.	Pernicious anemia.
		781—Urine.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
782—(a) Sputum, for tubercle bacilli. (b) Urine, for tubercle bacilli.	(a) Negative.* (b) Negative.*	812—Urine.	Negative.*
783—Blood, for Widal's reaction.	Negative.*	813—Blood examination.	Negative *
784—Urine.	Albuminuria.	814—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus infection.
785—Sputum, for tubercle bacilli.	Negative.*	815—Tumor from breast, for histologic diagnosis.	Cystic fibro-adenoma.
786—Blood examination.	Symptomatic anemia.	816—Tissue from anterior wall of vagina, for histologic diagnosis.	Negative.*
787—Growth from vocal band, for histologic diagnosis.	Inflammatory tissue.	817—Sputum, for tubercle bacilli.	Present.
788—Tumor from right breast, for histologic diagnosis.	Fibroadenoma.	818—Sputum, for tubercle bacilli.	Negative.*
789—Urine.	Albuminuria and tubercle bacilli.	819—Urine.	Negative *
790—Sputum, for tubercle bacilli.	Negative.*	820—Spreads from corneal ulcer, for bacteriologic examination.	No bacteria demonstrable.
791—Sputum, for tubercle bacilli.	Negative.*	821—Urine.	Albuminuria.
792—Sputum, for tubercle bacilli.	Negative.*	822—Kidneys, for histologic diagnosis.	Congenital cystic disease of the kidney.
793—Tissue from jaw, for histologic diagnosis.	Inflammatory tissue.	823—Urine.	Bile pigment.
794—Tumor from left breast, for histologic diagnosis.	Scirrhus carcinoma.	824—Fluid from pleural cavity, for bacteriologic examination.	Diplococcus of Sternberg.
795—Cervix, for histologic diagnosis.	Hyperplasia of cervix uteri.	825—Spreads from conjunctiva, for bacteriologic examination.	No bacteria demonstrable.
795½—Blood examination.	Chlorotic anemia.	826—Tissue from uterus, for histologic diagnosis.	Report not submitted.
796—Sputum, for tubercle bacilli.	Negative.*	827—Tissue from uterus, for histologic diagnosis.	Report not submitted.
797—Urine.	Albuminuria	828—Sections of nerve, for histologic diagnosis.	Interstitial neuritis.
798—Secretion from uterus, for bacteriologic examination.	Staphylococcus infection.	829—Gastric contents, for hydrochloric and lactic acids.	Negative.*
799—Wall of sinus, for histologic diagnosis.	Tuberculosis.	830—Stone from bladder, for histologic diagnosis.	Uric acid and calcium phosphate.
800—Sputum, for tubercle bacilli.	Negative.*	831—Tissue from alveolar process, for histologic diagnosis.	Squamous cell epithelioma.
801—Blood examination.	Negative.*	832—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.
802—Great toe, for histologic diagnosis.	Tuberculosis arthritis.	833—Spreads from conjunctiva, for bacteriologic examination.	Diplococcus of Sternberg.
803—Urine.	Albuminuria.	833½—Specimen from suspected case of yellow fever, for bacteriologic examination.	Bacillus icteroides could not be demonstrated.
804—Contents of cyst of frontal sinus, for bacteriologic examination.	Staphylococcus infection.	834—Growth from upper lip, for histologic diagnosis.	Report not submitted.
805—Spreads from corneal ulcer, for bacteriologic examination.	Negative.*	835—Tumor from left cheek, for histologic diagnosis.	Report not submitted.
806—Blood examination.	Negative.*	836—Left half of superior maxilla, for histologic diagnosis.	Report not submitted.
807—Spreads from conjunctiva, for bacteriologic examination.	No bacteria demonstrable.	837—Blood examination.	Negative.*
808—Organs from postmortem, for histologic examination.	Report not submitted.	838—Specimen from tibia, for histologic diagnosis.	Report not submitted.
809—Ovary and tube, for histologic diagnosis.	Specimens lost.		
810—Urine.	Negative.*		
811—Urine.	Specimen unfit for examination.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
839—Tissue from sternum, for histologic diagnosis.	Report not submitted.	870—Blood, for malaria organisms.	Present.
840—Appendix vermiformis, for histologic diagnosis.	Appendicitis.	871—Spreads from vaginal discharge, to determine presence of gonococci.	Not demonstrable.
841—Testicle, for histologic diagnosis.	Report not submitted.	872—Blood examination.	Simple anemia.
842—Tumor from ascending colon, for histologic diagnosis.	Inflammatory tissue.	873—Uterus, for histologic diagnosis.	Report not submitted.
843—Tumor from lower jaw, for histologic diagnosis.	Report not submitted.	874—Left eye, for histologic diagnosis.	Material unfit for examination.
844—Mass from upper jaw, for histologic diagnosis.	Report not submitted.	875—Urine.	Albuminuria.
845—Pleural effusion, for bacteriologic examination.	No bacteria demonstrable.	876—Aneurism of popliteal space, for histologic diagnosis.	Report not submitted.
846—Blood examination.	Negative.*	877—Cyst from neck, for histologic diagnosis.	Report not submitted.
847—Sputum, for tubercle bacilli.	Present.	878—Blood examination.	Negative.*
848—Aneurismal sac, for histologic diagnosis.	Nothing but blood clot demonstrable.	879—Growth from face, for histologic diagnosis.	Squamous epithelioma.
849—Blood examination.	Chlorotic anemia	880—Inoculation from nail, for bacteriologic examination.	Sterile.
850—Blood, for Widal's reaction.	Positive.	881—Uterus, for histologic diagnosis.	Myoma.
851—Pleural effusion, for tubercle bacilli.	Negative.*	882—Pus from appendicular abscess, for tubercle bacilli.	Negative.*
852—Pus from urethra, for bacteriologic examination.	Gonococcus.	883—Fluid obtained by lumbar puncture, for bacteriologic examination.	Diplococcus of Sternberg.
854—Breast and glands, for histologic diagnosis.	Report not submitted.	884—Right breast, for histologic diagnosis.	Scirrhus cancer.
855—Sputum, for tubercle bacilli.	Present.	885—Inoculation from leg, to determine character of infection.	Staphylococcus pyogenes albus.
856—Gland from neck, for histologic examination.	Report not submitted.	886—Leg, thigh, and sciatic nerve, for histologic diagnosis.	Gangrene.
857—Fluid from peritoneum, for bacteriologic examination.	Inflammatory exudate.	887—Tissue from forearm, for histologic diagnosis.	Simple fibroma.
858—Sputum, for tubercle bacilli.	Present.	888—Placenta, for histologic diagnosis.	Infarction.
859—Blood examination.	Negative.*	889—Pancreas, for histologic diagnosis.	Interstitial pancreatitis.
860—Fluid from ovarian cyst, for bacteriologic examination.	Negative.*	890—Sputum, for tubercle bacilli.	Present.
861—Fluid from hydronephrosis, for bacteriologic examination.	Material unfit for examination.	891—Sputum, for tubercle bacilli.	Present.
862—Inoculation from ovaries and tubes, to determine character of infection.	Gonococcus.	892—Portion of sciatic nerve, for histologic diagnosis.	Fibroma of nerve.
863—Tumor from rectum, for histologic diagnosis.	Report not submitted.	893—Blood examination.	Negative.*
864—Testicle, for histologic examination.	Inflammatory tissue.	894—Blood examination.	Negative.*
865—Cyst from ovary, for histologic diagnosis.	Report not submitted.	895—Inoculation from ear, to determine character of infection.	Diplococcus of Sternberg.
866—Entire left breast, for histologic diagnosis.	Report not submitted.	896—Liver, for histologic diagnosis.	Carcinoma.
867—Cyst wall from broad ligament and ovary, for histologic diagnosis.	Report not submitted.	897—Sputum, for tubercle bacilli.	Present.
868—Sputum, for tubercle bacilli.	Negative.*	898—Gall stones.	Carbonate of lime and cholesterol.
869—Sputum, for tubercle bacilli.	Negative.*		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
899—Inoculation from gall duct, to determine character of infection.	Sterile.	927—Urine.	Glycosuria.
900—Urine, for tubercle bacilli.	Present.	928—Blood, for malaria organ- isms.	Negative.*
901—Sputum, for tubercle bacilli.	Negative.*	929—Blood examination.	Negative.*
902—Blood examination.	Negative.*	930—Breast, for histologic diag- nosis.	Scirrhus carcinoma.
903—Fluid from cyst of breast, for bacteriologic examination.	No bacteria demonstrable.	931—Blood examination.	Negative.*
904—Blood examination.	Negative.*	932—Specimens from postmortem for bacteriologic examina- tion.	Pyogenic infection.
905—Mammary cyst, for histo- logic diagnosis.	Involution cyst.	933—Urine.	Negative.*
906—Dressing saturated with dis- charge from gall bladder, for bacteriologic examination.	Contains bile, no bacteria present.	934—Breast, for histologic diag- nosis.	Scirrhus carcinoma.
907—Debris removed from pelvis, for histologic diagnosis.	Inflammatory tissue.	935—Nerves, for histologic diag- nosis.	Report pending.
908—Fluid from pleural cavity, for tubercle bacilli.	Negative.*	936—Tissue from breast, for his- tologic diagnosis.	Paget's disease.
909—Discharge from bowel, for tubercle bacilli.	Not demonstrable.	937—Urine.	Negative.*
910—Spreads from secretion from eye, for bacteriologic exam- ination.	Diplococcus of Sternberg.	938—Blood examination.	Negative.*
911—Gall stones.	Carbonate of lime and cholesterol.	939—Sputum, for tubercle bacilli.	Negative.*
912—Sputum, for tubercle bacilli.	Present.	940—Tumor from temple, for his- tologic diagnosis.	Myxosarcoma, invol- ving parotid gland.
913—Urine, for tubercle bacilli.	Negative.*	941—Urine, for tubercle bacilli.	Present.
914—Gastric contents. (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative reac- tion. (b) Positive reaction.	942—Material from postmortem, for histologic diagnosis.	Thrombosis of right saphenous vein.
915—Material washed from ab- dominal wound, for histo- logic diagnosis.	Blood clot.	943—Right breast, for histologic diagnosis.	Scirrhus carcinoma.
916—Gall stones.	Carbonate of lime and cholesterol.	944—Urine.	Negative.*
917—Blood examination.	No report sub- mitted.	945—Kidney, for histologic diag- nosis.	Hydronephrosis.
918—Blood examination.	Negative.*	946—Blood examination.	Negative.*
919—Blood examination.	Negative.*	947—Inoculation from throat, to determine character of infec- tion.	Diplococcus of Sternberg.
920—Tumor from axilla, for his- tologic diagnosis.	Tuberculous lymphadenitis.	948—Lung, for histologic diag- nosis.	Croupous Pneumonia.
921—Specimen from postmortem, for histologic diagnosis.	Eclampsia.	949—Hypophysis cerebri, for his- tologic diagnosis.	Normal.
922—Culture tube inoculations, to determine character of in- fection.	Staphylococcus pyogenes albus.	950—Material from postmortem, for histologic diagnosis.	Millary tuberculosis.
923—Tumor from omentum, for histologic diagnosis.	Report not sub- mitted.	951—Blood, for malaria organ- isms.	Negative.*
924—Tumor from forearm, for histologic diagnosis.	Lipoma.	952—Tissue from uterus, for his- tologic diagnosis.	Specimen mislaid.
925—Inoculation from eye, to de- termine character of infec- tion.	Sterile.	953—Cystic tumor from neck, for histologic diagnosis.	Esophageal diverticulum.
926—Goitre, for histologic diag- nosis.	Hyperplastic goitre.	954—Sputum, for tubercle bacilli.	Present.
		955—Gland from neck, for histo- logic diagnosis.	Secondary carci- noma (scirrhus).
		956—Part of chest, for histologic diagnosis.	Epithelioma.
		957—Tissue from mouth, for his- tologic diagnosis.	Inflammatory necrosis.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
958—Specimen from tunica vaginalis, for histologic diagnosis.	Aberrant testicular tissue.	989—Tissue from mouth, for histologic diagnosis.	Squamous-cell epithelioma.
959—Urine.	Glycosuria.	990—Gastric contents, for hydrochloric acid.	Negative.*
960—Inoculation from thigh, to determine character of infection.	Diplococcus of Sternberg.	991—Tissue from lower jaw, for histologic diagnosis.	Squamous-cell epithelioma.
961—Prepuce, for histologic diagnosis.	Paget's disease.	992—Blood examination.	Pernicious anemia.
962—Testicle, for histologic diagnosis.	Orchitis.	993—Gastric contents, for hydrochloric acid.	Positive.
963—Tissue from eye, for histologic diagnosis.	Tuberculosis.	994—Blood examination.	Negative.*
964—Tissue from beneath clavicle for histologic diagnosis.	Normal lymphatic gland.	995—Urine.	Albuminuria.
965—Urine, for tubercle bacilli.	Negative.*	996—Tissue from nose, for histologic diagnosis.	Inflammatory tissue.
966—Blood examination.	Pernicious anemia.	997—Urine.	Negative.*
967—Urine.	Albuminuria.	998—Three large veins, for histologic diagnosis.	Varicose veins.
968—Testicle, for histologic diagnosis.	Tuberculosis.	999—Urine.	Negative.*
969—Vein from axilla, for histologic diagnosis.	Phlebectasia.	1000—Inoculation from "bone-disease" following typhoid, to determine character of infection.	Mixed infection. Staphylococcus pyogenes aureus, sarcina citreus.
970—Urine.	Albuminuria.	1001—Urine.	Negative.*
971—Urine.	Negative.*	1002—Tissue from cheek, for histologic examination.	Report pending.
972—Urine.	Negative.*	1003—Urine, for tubercle bacilli.	Present.
973—Urine, for tubercle bacilli.	Present.	1004—Sputum, for tubercle bacilli.	Negative.*
974—Urine, for tubercle bacilli.	Negative.*	1005—Sputum, for tubercle bacilli.	Negative.*
975—Gland (?) from neck, for histologic diagnosis.	Esophageal diverticulum.	1006—Sputum, for tubercle bacilli.	Negative.*
976—Sputum, for tubercle bacilli.	Negative.*	1007—Inoculation from lip, to determine character of infection.	Saccharomyces albicans.
977—Tissue from uterus, for histologic diagnosis.	Adenoma.	1007½—Specimen from postmortem, for histologic diagnosis.	Bronchopneumonia.
978—Urine.	Negative.*	10.8—Inoculation from thigh, to determine character of infection.	Staphylococcus pyogenes albus.
979—Inoculation from fluid from lateral ventricles of brain, to determine character of infection.	Diplococcus of Sternberg.	1009—Specimen from liver, for histologic diagnosis.	Gumma.
980—Blood examination.	Pernicious anemia.	1010—Blood examination.	Pernicious anemia (?)
981—Urine.	Albuminuria.	1011—Blood examination.	Negative.*
982—Urine, for tubercle bacilli.	Negative.*	1012—Blood examination.	Pernicious anemia (?)
983—Three warts, for histologic diagnosis.	Angioma.	1013—Tissue from neck, for histologic diagnosis.	Squamous-cell epithelioma.
984—Urine.	Negative.*	1014—Eye, for histologic diagnosis.	Report pending.
985—Inoculation from neck, to determine character of infection.	Sterile.	1015—Eye, for histologic diagnosis.	Report pending.
986—Two pieces of gauze, for bacteriologic examination.	Diplococcus of Sternberg.	1016—Inoculation from contents of gall bladder, to determine character of infection.	Sterile.
987—Uterus, for histologic diagnosis.	Interstitial and submucous leiomyomata	1017—Testicle and vas, for histologic diagnosis.	Epididymitis.
988—Tissue from diverticulum of bladder, for histologic diagnosis.	Non-striated muscle fibre		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1018—Pleura, for histologic diagnosis.	Sarcoma.	1020—Sputum, for tubercle bacilli.	Negative.*
1019—Tissue from nose, for histologic diagnosis.	Beginnings squamous-cell epithelioma with associated pyogenic infection.	1021—Material from postmortem, for histologic diagnosis.	Pernicious anemia.
		1022—Inoculation from throat, to determine character of infection.	Diplococcus of Sternberg.

The following is a list of specimens and materials examined in the Laboratories during the year 1900 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1023—Blood examination.	Negative.*	1046—Sputum, for tubercle bacilli.	Negative.*
1024—Vaginal discharge, for bacteriologic examination.	Inflammatory fluid. (?)	1047—Inoculation, to determine character of infection.	Pneumococcus.
1025—Inoculation from breast milk, for bacteriologic examination.	Staphylococcus pyogenes albus.	1048—Sputum, for tubercle bacilli.	Negative.*
1026—Urine, for tubercle bacilli.	Negative.*	1049—Gastric contents, for hydrochloric acid.	Negative.*
1027—Urine, for tubercle bacilli.	Negative.*	1050—Gastric contents, for hydrochloric acid.	Negative.*
1028—Urine, for tubercle bacilli.	Negative.*	1051—Urine.	Diabetes.
1029—Tissue from breast, for histologic diagnosis.	Scirrhus carcinoma.	1052—Urine.	Albuminuria.
1030—Sputum, for tubercle bacilli.	Negative.*	1053—Sputum, for tubercle bacilli.	Negative.*
1031—Inoculation from hip joint, to determine character of infection.	Sterile.	1054—Urine.	Negative.*
1032—Right leg with tumor and enlarged gland, for histologic diagnosis.	Small round-cell sarcoma.	1056—(a) Blood, for malarial organisms. (b) Urine.	(a) Negative.* (b) Negative.*
1033—Blood examination.	Negative.*	1057—Tissue from vagina, for histologic diagnosis.	Granulation tissue.
1034—Sputum, for tubercle bacilli.	Present.	1058—Growth from left superior maxillary region, for histologic diagnosis.	Mixed cell sarcoma.
1035—Gland from axilla, for histologic diagnosis.	Inflammatory tissue.	1059—Inoculation from gland, to determine character of infection.	Sterile.
1036—Calculus.	Oxalates, urates and phosphates.	1060—Blood examination.	Negative.*
1037—Tissue from anus, for histologic diagnosis.	Round-cell sarcoma.	1061—Sputum, for tubercle bacilli.	Present.
1038—Growth from hand, for histologic diagnosis.	Squamous-cell epithelioma.	1062—Pleura and pleural effusion, for bacteriologic examination.	Tuberculosis with fibroid thickening of pleura.
1039—Tissue from pia mater, for histologic diagnosis.	Fibrous tissue	1063—Wart from ear, for histologic diagnosis.	Papilloma.
1040—Inoculation from cyst wall, for bacteriologic examination.	Sterile.	1064—Right kidney and ureter, for histologic diagnosis.	Renal and urethral tuberculosis with marked fibrous hyperplasia.
1041—Tissue from liver, for histologic diagnosis.	Encephaloid carcinoma.	1065—Sputum, for Charcot-Leyden crystals, and Curschmann's spirals.	Negative *
1042—Tissue from ovaries, fundus uteri and omentum, for histologic diagnosis.	Papillomatous carcinoma.	1066—Iodoform emulsion, to determine if infected.	Sterile.
1043—Celluloid thread.	Experimental study published	1067—Inoculation from gall-bladder, to determine character of infection.	Staphylococcus pyogenes aureus.
1044—Left breast and enlarged glands, for histologic diagnosis.	Giant-cell sarcoma.	1068—Specimen from intestine, for histologic diagnosis.	Material not suitable for examination.
1045—Urine, for tubercle bacilli.	Negative.*		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1069—Sputum, for tubercle bacilli.	Negative.*	1097—Sputum, for tubercle bacilli.	Negative.*
1070—Discharge from pulmonary abscess, for tubercle bacilli.	Present.	1098—Breast and glands from axilla, for histologic diagnosis.	Chronic indurative mastitis.
1071—Sputum, for tubercle bacilli.	Present.	1099—Nerve, for histologic diagnosis.	No pathologic lesion demonstrable.
1072—Sputum, for tubercle bacilli.	Negative.*	1100—Nerve, for histologic diagnosis.	No pathologic lesion demonstrable.
1073—Omentum and part of uterine myoma for histologic diagnosis.	Myoma of uterus and varicose veins of omentum.	1101—Blood examination.	Symptomatic anemia.
1074—Blood examination.	Symptomatic anemia.	1102—(a) Enlarged omental glands, for histologic diagnosis. (b) Inoculation from peritoneal fluid, to determine character of infection.	(a) Cylindric-cell carcinoma. (b) Sterile.
1075—Blood examination.	Negative.*	1103—(a) Material from metacarpal region, for histologic diagnosis. (b) Portion of metacarpal bone, for histologic diagnosis.	Tuberculosis.
1076—Breast and axillary glands, for histologic diagnosis.	Scirrhus carcinoma.	1104—Blood examination.	Symptomatic anemia.
1077—Urine.	Negative.*	1105—Blood examination.	Symptomatic anemia.
1078—Sputum, for tubercle bacilli.	Negative.*	1106—Blood examination.	Negative.*
1079—Blood examination.	Negative.*	1107—Gastric contents, for lactic acid.	Negative.*
1080—Breast, for histologic diagnosis.	Specimen unfit for examination.	1108—Spreads from ear, for tubercle bacilli.	Negative.*
1081—Urine.	Negative.*	1109—Sputum, for tubercle bacilli.	Negative.*
1082—Calculus.	Uric acid, calcium oxalate.	1110—Gastric contents.	Undigested food.
1083—Testicle, for histologic diagnosis.	Orchitis.	1111—Testicle, for histologic diagnosis.	Inflammatory tissue.
1084—Blood examination.	Negative.*	1112—Membrane from lower lid, for histologic diagnosis.	Chronic inflammation.
1085—Tissue from nose and gland in neck, for histologic diagnosis.	Angiosarcoma.	1113—Portion of omentum and growths from uterine appendages, for histologic diagnosis.	Papilliferous cystadenoma.
1086—Kidney, for anatomic diagnosis.	Aneurism of renal artery.	1114—Tissue from mouth and posterior nares, for histologic diagnosis.	Squamous-cell epithelioma.
1087—Specimen from abortion, for histologic diagnosis.	Spilled in process of examination.	1115—Spreads from urethral discharge, for bacteriologic examination.	Gonococci.
1088—Blood examination.	Inflammatory leukocytosis.	1116—Ovaries, tubes, and glands from axilla, for histologic diagnosis.	Scirrhus carcinoma.
1089—Urine.	Negative.*	1117—Axillary gland, for histologic diagnosis.	Scirrhus carcinoma. Secondary.
1090—Urine.	Pyuria.	1118—Blood examination.	Negative.*
1091—Blood examination.	Anemia.	1119—Breast, for histologic diagnosis.	Scirrhus carcinoma.
1092—Blood examination.	Negative.*		
1093—Sputum, for tubercle bacilli.	Negative.*		
1094—Blood examination.	Negative.*		
1095—Glands of neck, for histologic diagnosis.	Sarcoma.		
1096—Gastric contents, for hydrochloric acid.	Negative.*		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1120—Uterus, for histologic diagnosis.	Specimen lost.	1146—Sputum, for tubercle bacilli.	Negative.*
1121—Gland from neck, for histologic diagnosis.	Specimen lost.	1147—Kidney, for histologic diagnosis.	Angiosarcoma (melanotic)
1122—Gland from jaw, for histologic diagnosis.	Inflammatory infiltration.	1148—Organs from postmortem, for anatomic diagnosis.	Aneurism of abdominal aorta.
1123—Gastric contents, for hydrochloric and lactic acids.	Present.	1149—Organs from postmortem, for histologic diagnosis.	Syncytioma malignum.
1124—Inoculation from mastoid, to determine character of infection.	Diplococcus of Sternberg.	1150—Blood examination.	Negative.*
1125—Urine.	Albuminuria.	1151—Blood examination.	Negative.*
1126—Penis, for histologic diagnosis.	Specimen unfit for examination.	1152—Goitre, for histologic diagnosis.	Cystic goitre.
1127—Blood examination.	Pernicious anemia (?)	1153—Foot and ankle, for histologic diagnosis.	Tuberculosis.
1128—Fallopian tube, for histologic diagnosis.	Tuberculous salpingitis.	1154—Tumor from thigh, for histologic diagnosis.	Fibroma.
1129—Tumor of parotid gland for histologic diagnosis.	Carcinoma.	1155—Blood examination.	Negative.*
1130—Urine.	Diabetes mellitus.	1156—Blood examination.	Chlorosis.
1131—Sputum, for tubercle bacilli.	Present.	1157—Sputum, for tubercle bacilli.	Negative.*
1132—Sputum, for tubercle bacilli.	Negative.*	1158—Sputum, for tubercle bacilli.	Negative.*
1133—Inoculation from abscess, to determine character of infection.	Staphylococcus pyogenes aureus.	1159—Urine, for tubercle bacilli.	Negative.*
1134—Rectum, sacrum and coccyx, for histologic diagnosis.	Cylindric-cell carcinoma.	1160—Sputum, for tubercle bacilli.	Present.
1135—Sputum, for tubercle bacilli.	Present.	1161—Ganglion of wrist, for histologic diagnosis.	Exudation cyst.
1136—Fluid from pleural sac, for bacteriologic examination.	Negative.	1162—Inoculation from wrist, to determine character of infection.	Sterile.
1137—Sputum, for tubercle bacilli.	Present.	1163—Tissue from mouth, for histologic diagnosis.	Granulation tissue.
1138—Sputum, for Charcot-Leyden crystals, and Curschmann's spirals.	Negative.*	1164—Vaginal growth, for histologic diagnosis.	Specimen unfit for examination.
1139—Mass from left groin, for histologic diagnosis.	Chronic inflammation.	1165—Tumor from anterior cervical triangle, for histologic diagnosis.	Myxosarcoma.
1140—Sputum, for tubercle bacilli.	Negative.*	1166—Piece of tongue, for histologic diagnosis.	Hypertrophied papilla.
1141—Inoculation from aneurism, to determine character of infection.	Sterile.	1167—Blood examination.	Symptomatic anemia.
1142—Urine, for tubercle bacilli.	Negative.*	1168—Blood examination.	Pernicious anemia. (?)
1143—Gastric contents, (a) for hydrochloric acid, (b) for lactic acid.	(a) Negative.* (b) Present.	1169—Tissue from lower lip, for histologic diagnosis.	Squamous-cell epithelioma.
1144—Urine.	Negative.*	1170—Sputum, for tubercle bacilli.	Negative.*
1145—Gastric contents, for hydrochloric acid.	Present.	1171—Uterine scrapings, for histologic diagnosis.	Cylindric-cell carcinoma.
		1172—Pleural effusion, for bacteriologic examination.	Sterile.
		1173—Sputum, for tubercle bacilli.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1174—Urine.	Diabetes mellitus.	1198—Urine, for tubercle bacilli.	Present.
1175—Sputum, for tubercle bacilli.	Present.	1199—Blood examination.	Symptomatic anemia.
1176—Inoculations from appendix, to determine character of infection.	Bacillus coli communis.	1200—Sputum, for tubercle bacilli.	Negative.*
1177—Tumor from nose, for histologic diagnosis.	Granulation tissue.	1201—Left testicle, for histologic diagnosis.	Tuberculosis.
1178—Inoculation from pleural cavity, to determine character of infection.	Sterile.	1202—Sputum, for tubercle bacilli.	Negative.*
1179—Inoculation from arm, to determine character of infection.	Pure culture bacillus prodigiosus.	1203—Tonsil, for histologic diagnosis.	Suppurative tonsillitis.
1180—Breast and gland, for histologic diagnosis.	Cystic mammary gland with interstitial mastitis.	1204—Appendix, for histologic diagnosis.	Chronic indurative appendicitis.
1181—Organs from postmortem, for histologic diagnosis.	Aneurism of thoracic aorta.	1205—Inoculation and spreads from hand, to determine character of infection.	Staphylococcus pyogenes albus and staphylococcus pyogenes aureus
1182—Breast, for histologic diagnosis.	Interstitial inflammation with cyst formation.	1206—Urine, for tubercle bacilli.	Negative.*
1183—Gastric contents, for hydrochloric acid.	Present.	1207—Sputum, for tubercle bacilli.	Negative.*
1184—Inoculation from discharge from ear, to determine character of infection.	Pneumococcus.	1208—Urine, for tubercle bacilli.	Negative.*
1185—Mass of tissue from appendix, for histologic diagnosis.	Granulation tissue.	1209—Breast, for histologic diagnosis.	Intracanalicular papilloma.
1186—Inoculation from discharge from hand, to determine character of infection.	Micrococcus pyogenes albus.	1210—Glands from clavicle, for histologic diagnosis.	Lymphadenitis.
1187—Blood examination.	Pernicious anemia. (?)	1211—Inoculation from pharynx, to determine character of infection.	Diplococcus of Sternberg.
1188—Blood examination.	Pernicious anemia. (?)	1212—Left testicle, for histologic diagnosis.	Small round-cell sarcoma.
1189—Inoculation from ear, to determine character of infection.	Bacillus pyogenes foetidus. Micrococcus Pasteuri.	1213—Pleural effusion, for bacteriologic examination.	Bacillus megatherium.
1190—Sputum, for tubercle bacilli.	Negative.*	1214—Sputum, for tubercle bacilli.	Negative.*
1191—Sputum, for tubercle bacilli.	Negative.*	1215—Blood examination.	Anemia.
1192—Testicle, for histologic diagnosis.	Specimen spoiled in process of examination.	1216—Blood examination.	Anemia (Symptomatic)
1193—Tissue from cheek, for histologic diagnosis.	Squamous-cell epithelioma.	1217—Fluid from pleural cavity, for bacteriologic examination.	Negative.*
1194—Tumor of uterus, for histologic diagnosis.	Myoma with some myxoid degeneration.	1218—Pleural effusion, for tubercle bacilli.	Negative.*
1195—Inoculation from gall bladder, to determine character of infection.	Staphylococcus Pyogenes albus.	1219—Inoculation from left tonsil, to determine character of infection.	Staphylococcus pyogenes albus, diplococcus of Sternberg.
1196—Breast, for histologic diagnosis.	Chronic productive mastitis.	1220—Blood examination.	Anemia (Symptomatic)
1197—Blood examination.	Symptomatic anemia.	1221—Sputum, for tubercle bacilli.	Negative.*
		1222—Urine.	Diabetes mellitus.
		1223—Inoculation from eyes, to determine character of infection.	Diplobacillus.
		1224—Placenta and membranes, for histologic diagnosis.	Placental infarction.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1225—Gastric contents, for hydrochloric acid.	Present.	1250—Urine.	Negative.*
1226—Tissue from chin and neck, for histologic diagnosis.	Squamous-cell epithelioma.	1251—Breast and contents of axilla, for histologic diagnosis.	Scirrhus.
1227—Uterus, for histologic diagnosis.	Squamous-cell epithelioma.	1252—Breast and axillary and supraclavicular glands, for histologic diagnosis.	Scirrhus carcinoma.
1228—Sputum, for tubercle bacilli.	Negative.*	1253—Inoculation from mastoid, to determine character of infection.	Staphylococcus pyogenes aureus.
1229—Gastric contents.	Negative.*	1254—Tissue from superior maxilla, for histologic diagnosis.	Squamous-cell epithelioma.
1230—Cyst from vaginal wall, for histologic diagnosis.	Cyst of Gärtner's duct.	1255—Inoculation from knee-joint, to determine character of infection.	Sterile.
1231—Uterine polyp, for histologic diagnosis.	Myoma.	1256—Inoculations, (a) from right eye. (b) from left eye, to determine character of infection.	(a) Staphylococcus pyogenes aureus. (b) Staphylococcus pyogenes albus.
1232—Inoculation from right breast, to determine character of infection.	Sterile.	1257—Lymphatic gland from femoral region, for histologic diagnosis.	Columnar-cell carcinoma. Secondary.
1233—Urine, for tubercle bacilli.	Present.	1258—Breast, for histologic diagnosis.	Scirrhus carcinoma.
1234—Toe, for histologic diagnosis.	No abnormality found.	1259—Tissue from right knee-joint, for histologic diagnosis.	Inflammatory tissue.
1235—Ovarian tumor, for histologic diagnosis.	Papillary cancer.	1260—Tissue from neck, for histologic diagnosis.	Tubercular granulation tissue.
1236—Urine.	Albuminuria.	1261—Tumor, for histologic diagnosis.	Squamous-cell epithelioma.
1237—Breast, for histologic diagnosis.	Adeno-fibroma (cystic) with beginning carcinoma.	1262—Tubes and ovaries, for histologic diagnosis.	Tuberculosis.
1238—Tumor from neck, for histologic diagnosis.	Epithelioma (squamous-cell)	1263—Pleural effusion, for tubercle bacilli.	Negative.*
1239—Testicle, for histologic diagnosis.	Material unfit for examination.	1264—Urine.	Negative.*
1240—Tissue from breast, for histologic diagnosis.	Specimen spoiled in process of examination.	1265—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Positive. (b) Negative.
1241—Tumor from breast, for histologic diagnosis.	Adeno-fibroma (cystic)	1267—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Positive.
1242—Inoculation from gall bladder, to determine character of infection.	Sterile.	1268—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
1243—Inoculation from metacarpal bone, to determine character of infection.	Negative.*	1269—Gastric contents, for hydrochloric acid.	Present.
1244—Breast and axillary glands, for histologic diagnosis.	Scirrhus carcinoma.	1270—Milk, for tubercle bacilli.	Negative.*
1245—Pleural effusion, for bacteriologic examination.	Diplococcus of Sternberg.	1271—Inoculation, to determine character of infection.	Staphylococcus pyogenes albus.
1246—Sputum, for tubercle bacilli.	Negative.*	1272—Blood, for Widal's test.	Positive.
1247—(a) Tissue from leg, for histologic diagnosis. (b) Inoculation from leg, to determine character of infection.	(a) Granulation tissue. (b) Staphylococcal infection.	1273—Blood, for Widal's test.	Negative.*
1248—Gland from neck, for histologic diagnosis.	Fibroma.	1274—Blood, for Widal's test.	Positive.
1249—Urine.	Negative.*		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1275—Blood, for Widal's test.	Positive.	1300—Urine.	Diabetes mellitus.
1276—Blood, for Widal's test.	Negative.*	1301—Gastric contents, for hydrochloric acid.	Positive.
1277—Right breast, for histologic diagnosis.	Fibro-adenoma.	1302—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Positive.
1278—Urine, for tubercle bacilli.	Negative.*	1303—Breast, for histologic diagnosis.	Endothelioma.
1279—Urine.	Negative.*	1304—Inoculation from lip, to determine character of infection.	Pyogenic infection.
1280—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Positive.	1305—Appendix, for histologic diagnosis.	Appendicitis.
1281—Tonsil, for histologic diagnosis.	Tonsillitis.	1306—Inoculation from ear, to determine character of infection.	Bacillus proteus.
1282—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative * (b) Positive	1307—Blood, for Widal's test.	Negative.*
1283—Sputum, for tubercle bacilli.	Negative.*	1308—Blood, for Widal's test.	Positive.
1284—Inoculation from ear, to determine character of infection.	Pneumococcus and bacillus diphtheriae.	1309—Gastric contents, for hydrochloric acid.	Positive.
1285—Inoculation from vaginal secretion, to determine character of infection.	Staphylococcus pyogenes aureus.	1310—Tumor from bladder, for histologic diagnosis.	Villous papilloma.
1286—Small piece of membrane from throat, for diphtheria bacilli.	Bacillus diphtheriae.	1311—Sputum, for tubercle bacilli.	Negative.*
1287—Vaginal discharge, for bacteriologic examination.	Proteus and Staphylococcus pyogenes aureus.	1312—Gastric contents, for hydrochloric acid.	Positive.
1288—Inoculation from ulcer, to determine character of infection.	Staphylococcus pyogenes aureus.	1313—Inoculation, to determine character of infection.	Staphylococcus pyogenes aureus.
1289—Urine.	Spermatorrhoea.	1314—Blood, for Widal's test.	Negative.*
1290—Tissue from ulcer, for histologic diagnosis.	Specimen unfit for examination.	1315—Blood, for Widal's test.	Negative.*
1291—Blood, for Widal's test.	Negative.*	1316—Blood examination.	Negative.*
1292—Toe, for histologic diagnosis.	Inflammatory tissue.	1317—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Positive
1293—Gland from axilla, for histologic diagnosis.	Lymphatic gland.	1318—Tumor from chest, for histologic diagnosis.	Spindle-cell sarcoma.
1294—Cystic breast, for histologic diagnosis.	Cystic fibro-adenoma.	1319—Testicle, for histologic diagnosis.	Carcinoma.
1295—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Positive.	1320—Blood, for Widal's test.	Positive.
1296—Inoculation from throat, for diphtheria bacilli.	Bacillus diphtheriae.	1321—Inoculation from abdominal wound, to determine character of infection.	Staphylococcus pyogenes aureus.
1297—Uterus, for histologic diagnosis.	Fibroma.	1322—Inoculation from skin, to determine character of infection.	Staphylococcus pyogenes aureus.
1298—Breast, for histologic diagnosis.	Scirrhus carcinoma.	1323—Right breast, for histologic diagnosis.	Chronic interstitial mastitis.
1299—Cystic and atrophied ovary, for histologic diagnosis.	Fibroid oöphoritis.	1324—Inoculation from tonsil, to determine character of infection.	Staphylococcus pyogenes albus.
		1325—Tumor from intestine, for histologic diagnosis.	Cylindric-cell carcinoma.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1326—Inoculation and spreads, to determine character of infection.	Staphylococcus pyogenes aureus.	1350—Gastric contents, for hydrochloric acid.	Positive.
1327—Breast, for histologic diagnosis.	Chronic productive interstitial mastitis.	1351—Inoculation and spreads from blood, to determine character of infection.	No bacteria demonstrable.
1328—Inoculation from abscess, to determine character of infection.	Staphylococcus pyogenes aureus.	1352—Spreads from conjunctiva, for bacteriologic examination.	Bacillus of Weeks.
1329—Tissue from sinus of groin, for histologic diagnosis.	Tuberculosis.	1353—Urine, for lead.	Positive.
1330—Tumor from hip, for histologic diagnosis.	Chondroma.	1354—Inoculation from throat, to determine character of infection.	Bacillus diphtheriæ. Staphylococcus pyogenes aureus.
1331—Upper jaw, for histologic diagnosis.	Papillary carcinoma.	1355—Breast, for histologic diagnosis.	Mixed-cell sarcoma.
1332—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Positive.	1356—Inoculation from breast, to determine character of infection.	Sterile.
1333—Gastric contents, (a) for hydrochloric acid. (b) for lactic acid.	(a) Negative.* (b) Present.	1357—Tumor of broad ligament, for histologic diagnosis.	Mixed-cell sarcoma.
1334—Inoculation from throat, to determine character of infection.	Diplococcus of Sternberg.	1358—Brain tumor, for histologic diagnosis.	Examination not completed.
1335—Breast, for histologic diagnosis.	Scirrhus carcinoma.	1359—Urine.	Diabetes mellitus.
1336—Inoculation from vaginal secretion, to determine character of infection.	Staphylococcus pyogenes albus.	1360—Urine, for tubercle bacilli.	Present.
1337—Tumor from anus, for histologic diagnosis.	Adenoma.	1361—Blood, for bacteriologic examination.	Staphylococcus pyogenes albus.
1338—(a) Urine. (b) Sputum.	(a) Negative.* (b) Streptococci.	1362—Cervix and body of uterus, for histologic diagnosis.	Mixed-cell sarcoma.
1339—Sputum, for tubercle bacilli.	Present.	1363—Inoculation from throat, to determine character of infection.	Pneumococcus.
1340—Inoculation from throat, for diphtheria bacilli.	Negative.*	1364—Gland from neck, for histologic diagnosis.	Tuberculous lymphadenitis.
1341—Fluid from breast, for bacteriologic examination.	Negative.*	1365—Spreads from conjunctiva, for bacteriologic examination.	Negative.*
1342—Inoculation and spreads from vaginal secretion, to determine character of infection.	Staphylococcus pyogenes albus.	1366—Spreads from conjunctiva, for bacteriologic examination.	Koch-Weeks bacillus.
1343—Growth from toe, for histologic diagnosis.	Squamous-cell epithelioma.	1367—Blood, for bacteriologic examination.	Negative.*
1344—Tissue from breast, for histologic diagnosis.	Scirrhus carcinoma.	1368—Inoculation from gall bladder, to determine character of infection.	Negative.*
1345—Gastric contents, for blood.	Negative.*	1369—Tumor from anus, for histologic diagnosis.	Cylindric-cell carcinoma.
1346—Inoculation from spinal fluid, to determine character of infection.	Diplococcus of Sternberg.	1370—(a) Inoculation from breast, to determine character of infection. (b) Material from breast cavity, for bacteriologic examination.	(a) Staphylococcus pyogenes albus. (b) Staphylococcus pyogenes albus.
1347—Gastric contents.	Partly digested muscle.	1371—Organs from postmortem, for histologic diagnosis.	Rupture of spleen and liver.
1348—Inoculation from vaginal secretion, to determine character of infection.	Bacillus coli communis.	1372—Organs from postmortem, for histologic diagnosis.	Pneumococcal meningitis.
1349—Inoculation from breast, to determine character of infection.	Staphylococcus pyogenes aureus.	1373—Gall stones.	Cholesterin.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1374—Urine.	Parenchymatous nephritis.	1401—Appendix, for histologic diagnosis.	Study not completed.
1375—Blood, for Widal's test.	Positive.	1402—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
1376—Urethral calculus.	Phosphatic.	1403—Tissue from neck, for his- tologic diagnosis.	Study not completed.
1377—Fluid removed by aspira- tion, for bacteriologic ex- amination.	Negative.*	1404—Blood, for Widal's test.	Negative.*
1378—Breast and glands, for his- tologic diagnosis.	Scirrhus carcinoma.	1405—Small tumor from elbow, for histologic diagnosis.	Study not completed.
1379—Bone, for histologic diag- nosis.	Beginning absorption.	1406—Gastric contents, for hydro- chloric acid.	Positive.
1380—Kidney, for histologic diag- nosis.	Cystic disease of the kidney.	1407—Tissue from left iliac fossa, for histologic diagnosis.	Study not completed.
1381—Tissue from mouth, for carcinoma.	Negative.*	1408—Inoculation from hand, to determine character of in- fection.	Sterile.
1382—Growth from eye-lid, for histologic diagnosis.	Granulation tissue.	1409—Inoculation from neck, to determine character of in- fection.	Staphylococcus pyogenes albus.
1383—Enlarged gland from mes- ocolon, for histologic diag- nosis.	Lymphadenitis.	1410—Growth from eyelid, for histologic diagnosis.	Granulation tissue.
1384—Blood examination.	Negative.*	1411—Blood, for Widal's test.	Negative.*
1385—Blood, for Widal's test.	Negative.*	1412—Calculi.	Uric acid and phosphates.
1386—Mass from tongue, for his- tologic diagnosis.	Squamous-cell epithelioma.	1413—(a) Gall stones. (b) Shreds of tissue, for histologic diagnosis.	(a) Cholesterin. (b) Necrotic tissue.
1387—Swabs from throat, for diphtheria bacilli.	Negative.*	1414—Inoculation from gall blad- der, to determine character of infection.	Bacillus coli communis.
1388—Urine.	Albuminuria.	1415—Inoculation from urine, to determine character of in- fection.	Bacillus coli com- munis; urobacillus Pasteuri; staphylo- coccus pyogenes al- bus.
1389—Inoculation from throat, to determine character of in- fection.	Streptococcus infection.	1416—Right kidney, for histologic diagnosis.	Study not completed.
1390—Inoculation from bile, to determine character of in- fection.	Staphylococcus pyogenes albus.	1417—Inoculation from hip-joint, to determine character of infection.	Bacillus pyocyaneus; staphylococcus pyo- genes aureus.
1391—Testicle, for histologic diag- nosis.	Study not completed.	1418—Gastric contents, for hydro- chloric acid.	Present.
1392—Tumor from arm, for histo- logic diagnosis.	Tuberculosis.	1419—Urine.	Negative.*
1393—Tumor from jaw, for histo- logic diagnosis.	Squamous-cell epithelioma.	1420—Tissue from leg, for bacteri- ologic diagnosis.	Tetanus.
1394—Appendix, for histologic diagnosis.	Appendicitis.	1421—Organs from postmortem, for histologic diagnosis.	Carcinomatosis.
1395—Inoculation from gall blad- der, to determine character of infection.	Sterile.	1422—Bony mass from tibia, for histologic diagnosis.	Normal bone.
1396—Blood, for Widal's test.	Negative.*	1423—Lobe of ear, for histologic diagnosis.	Squamous-cell epithelioma.
1397—Spreads from eye, for bac- teriological examination.	Diplococcus and diplobacillus.	1424—Blood, for Widal's test.	Positive.
1398—Gall stones.	Study not completed.	1425—Blood, for Widal's test.	Positive.
1399—Blood, for bacteriologic ex- amination.	Sterile.		
1400—Three masses from rectum, for histologic diagnosis.	Cylindric-cell carcinoma.		

The following is a list of specimens and materials examined in the Laboratories during the year 1901 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1426—Gastric contents, for hydrochloric acid.	Negative *	1447—Blood, for Widal's test.	Negative.*
1427—Pleural effusion, for tubercle bacilli.	Negative.*	1448—Gastric contents, for hydrochloric acid.	Positive.
1428—Inoculation from neck, to determine character of infection.	Staphylococcus pyogenes aureus.	1449—Gastric contents, for hydrochloric acid.	Negative.*
1429—Inoculation from leg, to determine character of infection.	Sterile.	1450—Blood, for Widal's test.	Negative.*
1430—Bone from leg, for histologic diagnosis.	Ossifying myositis.	1451—Bone from skull, for histologic diagnosis.	Necrosis.
1431—Cast from colon.	Membranous colitis.	1452—Inoculation from abdominal cavity, to determine character of infection.	Bacillus coli communis; staphylococcus pyogenes aureus.
1432—Tissue, for histologic diagnosis.	Large and small round cell sarcoma with areas of myxomatous degeneration.	1453—Adrenal, for histologic diagnosis.	Tuberculosis.
1433—Tissue from forehead, for histologic diagnosis.	Squamous cell epithelioma.	1454—Inoculations from (a) right eye, (b) left eye, to determine character of infection.	(a) Xerosis bacillus; (b) xerosis bacillus; staphylococci pyogenes aureus and albus.
1434—Cyst from neck, for histologic diagnosis.	Branchial cyst.	1455—Urine.	Glycosuria.
1435—Tumor from face, for histologic diagnosis.	Squamous cell epithelioma.	1456—Blood examination.	Leukopenia.
1436—Gastric contents, for hydrochloric acid.	Negative.*	1457—Breast, for histologic diagnosis.	Suppurative mastitis.
1437—(a) Sputum, for tubercle bacilli. (b) Urine.	(a) Negative.* (b) Albuminuria.	1458—Clots from bladder, for histologic diagnosis.	Infected coagula.
1438—Testicle, for histologic diagnosis.	Chronic, caseous, tuberculous orchitis.	1459—Sections of mammary gland, for histologic diagnosis.	Spindle cell sarcoma.
1439—Ulcer from anus, for histologic diagnosis.	Inflammatory and necrotic tissue.	1460—Glands from neck, for histologic diagnosis.	Lymphadenoid tuberculosis.
1440—Testicle, for histologic diagnosis.	Undescended, hyoplastic testicle showing interstitial hemorrhage.	1461—Inoculation from gall bladder, to determine character of infection.	Bacillus coli communis.
1441—Sputum, for tubercle bacilli.	Negative.*	1462—Lung, for histologic diagnosis.	Gumma.
1442—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	1463—Lung, for histologic diagnosis.	Croupous pneumonia.
1443—Tissue from autopsy, for histologic diagnosis.	Sarcomatosis.	1464—(a) Tissue from eye, for histologic diagnosis. (b) Inoculation from eye, to determine character of infection.	(a) Suppurative inflammation. (b) Micrococcus pyogenes aureus, Bacillus coli communis; pneumococcus; staphylococcus pyogenes aureus.
1444—Adrenal, for histologic diagnosis.	Tuberculosis.	1465—Sections of prostate gland, for histologic diagnosis.	Adenoma.
1445—Blood, for Widal's test.	Negative.*	1466—Inoculation from arm, to determine character of infection.	Sterile.
1446—Inoculation from abscess of abdomen, to determine character of infection.	Staphylococcus pyogenes albus; bacillus subtilis.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1467—Inoculation, to determine character of infection.	Sterile.	1491—Breast, for histologic diagnosis.	Scirrhus carcinoma.
1468—Blood, for Widal's test.	Negative.*	1492—Inoculation from eye, to determine character of infection.	Sterile.
1469—Cyst wall from upper jaw, for histologic diagnosis.	Dentigerous cyst.	1493—Blood, for Widal's test.	Positive.
1470—Breast, for histologic diagnosis.	Pericanalicular fibroma.	1494—Inoculation from thigh, to determine character of infection.	Streptococcus pyogenes.
1471—Nerves from brachial plexus, also glands bordering on plexus, for histologic diagnosis.	Interstitial and farinomatous neuritis; secondary glandular carcinoma.	1495—Uterus, for histologic diagnosis.	Epithelioma.
1472—Blood, for Widal's test.	Positive.	1496—Inoculation from ascitic fluid, to determine character of infection.	Staphylococcus pyogenes albus; bacillus coli communis.
1473—Gastric contents, for lactic acid.	Positive.	1497—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
1474—Urine.	Normal.	1498—Inoculation from abdominal fluid, to determine character of infection.	Sterile.
1475—Pleural effusion, for tubercle bacilli.	Negative.*	1499—Inoculation from mastoid, to determine character of infection.	Streptococcus pyogenes.
1476—Tissue from femur, for histologic diagnosis.	Myxoma.	1500—Sputum, for tubercle bacilli.	Negative.*
1477—Lochia, for bacteriologic examination.	Sarcinae citreus; staphylococcus pyogenes aureus; Bacillus megatherium.	1501—Enucleated eye-ball, for histologic diagnosis.	Spindle cell sarcoma of choroid.
1478—Breast, for histologic diagnosis.	Chronic interstitial, interlobular and intralobular mastitis.	1502—Inoculation from right iliac region, to determine character of infection.	Sterile.
1479—Tissue from lip, for histologic diagnosis.	Endothelioma.	1503—Blood, for Widal's test.	Negative *
1480—Blood, for Widal's test.	Negative.*	1504—Uterus, for histologic diagnosis.	Fibromyoma.
1481—Inoculation from jaw, to determine character of infection.	Streptococcus pyogenes; staphylococcus pyogenes aureus. Staphylococcus pyogenes albus in pure culture.	1505—Lochia, for bacteriologic examination.	Micrococci of suppuration; staphylococcus pyogenes albus.
1482—Scrapings from uterus, for histologic diagnosis.	Epithelioma.	1506—Lower part of rectum, for histologic diagnosis.	Cylindric cell carcinoma.
1483—Prostate gland, for histologic diagnosis.	Adenoma.	1507—Blood, for Widal's test.	Negative.*
1484—Inoculation from eye, to determine character of infection.	Streptococcus pyogenes; pseudo-diphtheria bacillus.	1508—Heart, for histologic diagnosis.	Interstitial myocarditis.
1485—Lochia, for bacteriologic examination.	Staphylococcus pyogenes aureus.	1509—Uterus, for histologic diagnosis.	Fibromyoma.
1486—Inoculation from gall-bladder, to determine character of infection.	Bacillus coli communis.	1510—Lochia, for bacteriologic examination.	Staphylococci pyogenes albus and aureus; penicillium glaucum.
1487—Lochia, for bacteriologic examination.	Staphylococcus pyogenes albus.	1511—Contents of uterus, for histologic diagnosis.	Fibromyoma.
1488—Inoculation from eye, to determine character of infection.	Sterile.	1512—Inoculation from abdominal incision, to determine character of infection.	Bacillus coli communis; unidentified bacillus micrococci of suppuration; staphylococcus pyogenes aureus.
1489—Tissue from abdominal growth, for histologic diagnosis.	Papillary cystadenoma.	1513—Inoculation and spreads from neck, to determine character of infection.	Tubercle bacilli.
1490—Urine.	Negative.*		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1514—Tissue from neck, for histologic diagnosis.	Endothelioma.		(a) Bacillus coli communis; staphylococcus pyogenes aureus. (b) Micrococci of suppuration; the bacillus of Axenfeld and Morax; Diplococcus of Sternberg.
1515—Inguinal glands, for histologic diagnosis.	Lymphadenitis, and giant cell sarcoma.	1540—(a) Inoculation, (b) spreads from eye, to determine character of infection.	
1516—Blood, for Widal's test.	Negative.*		
1517—Blood, for Widal's test.	Negative.*	1541—(a) Inoculation, (b) spreads from eye, to determine character of infection.	(a) Staphylococcus pyogenes aureus. (b) Micrococci of suppuration.
1518—Solutions for bacteriologic examination.	Sarcinae citreus.	1542—Tissue from ulcer over tibia, for histologic diagnosis.	Squamous cell epithelioma.
1519—Blood, for Widal's test.	Negative.*	1543—Sputum, for tubercle bacilli.	Negative.*
1520—Spinal cord and nerves, for histologic diagnosis.	Syringo-myelia.	1544—Tumor from penis, for histologic diagnosis.	Squamous cell carcinoma.
1521—Mass from throat, for histologic diagnosis.	Proliferating papillary cystoma.	1545—Growth from cheek, for histologic diagnosis.	Papilloma.
1522—Sputum, for tubercle bacilli.	Present.	1546—Blood, for Widal's test.	Negative.*
1523—Intestine, for histologic diagnosis.	Chronic ulcerative colitis.	1547—Tissue from tongue, for histologic diagnosis.	Papilloma.
1524—Breast, for histologic diagnosis.	Chronic fibrous mastitis.	1548—Part of tongue, for histologic diagnosis.	Glandular cell carcinoma.
1525—Left Kidney, for histologic diagnosis.	Secondary cancer.	1549—Piece of bone, for histologic diagnosis.	Chronic suppurative osteitis.
1526—Breast, for histologic diagnosis.	Chronic fibrous mastitis.	1550—Urine.	Glycosuria.
1527—Testicle, for histologic diagnosis.	Suppurative orchitis.	1551—Glands from neck, for histologic diagnosis.	Large and small round cell sarcoma.
1528—(a) Gland from neck, (b) nerve, for histologic diagnosis.	(a) Scirrhus and encephaloid carcinoma of neck. (b) Chronic interstitial neuritis with degeneration.	1552—Lochia, for bacteriologic examination.	Staphylococcus pyogenes albus; staphylococcus pyogenes aureus; Aspergillus niger.
1529—Tissue from cicatrix over sternum for histologic diagnosis.	Inflammatory tissue.	1553—Tissue from rectum, for histologic diagnosis.	Not suitable for examination.
1530—Tissue from costal cartilage, for histologic diagnosis.	Granulation tissue.	1554—Urine, for tubercle bacilli.	Positive.
1531—Breast, for histologic diagnosis.	Adenofibroma.	1555—Glands from neck, for histologic diagnosis.	Tubercular lymphadenitis.
1532—Inoculation from costal cartilage, to determine character of infection.	Bacillus coli communis.	1556—Nail scrapings, for bacteriologic examination.	Infected.
1533—Fluid from spinal cord, for bacteriologic examination.	Negative.	1557—Gastric contents, for hydrochloric acid.	Negative.*
1534—Testicle, for histologic diagnosis.	Chronic, caseous, tuberculous orchitis.	1558—Tumor from forehead, for histologic diagnosis.	Cavernous hemangioma.
1535—Tissue from eye-lid, for histologic diagnosis.	Inflammatory tissue.	1559—Breast, for histologic diagnosis.	Papillary cystadenoma with beginning cancerous transformation.
1536—Tissue from forearm, for histologic diagnosis.	Tuberculosis.	1560—Testicle, for histologic diagnosis.	Caseous tuberculosis.
1537—Mass from eye, for histologic examination.	Purulent vitreous.	1561—Tumor from neck, for histologic diagnosis.	Telangiectatic sarcoma.
1538—Urine.	Albuminuria.	1562—Sputum, for tubercle bacilli.	Negative.*
1539—Solutions for bacteriologic examination.	Infected.	1563—Urine.	Albuminuria.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1564—Breast, for histologic diagnosis.	Acute, suppurative mastitis.	1584—Breast, for histologic diagnosis.	Endothelioma.
1565—Glands from axilla, for histologic diagnosis.	Tubercular lymphadenitis.	1585—Testicle, for histologic diagnosis.	Lost in preparation.
1566—Urine, for tubercle bacilli.	Negative.*	1586—Bone, for histologic diagnosis.	Tuberculosis.
1567—Liver, for histologic diagnosis.	Gumma.	1587—Gastric contents, for hydrochloric acid.	Positive.
1568—Inoculation from abdominal cavity, to determine character of infection.	Bacillus pyocyaneus and a bacillus of the colon group.	1588—Tissue from breast, for histologic diagnosis.	Peri, and intercanalicular fibroma.
1569—Gastric contents, for hydrochloric acid.	Positive.	1589—Sputum, for tubercle bacilli.	Positive.
1570—Lochia, for bacteriologic examination.	Staphylococcus pyogenes albus; micrococci of suppuration; sarcinae.	1590—Lochia, for bacteriologic examination.	Micrococci of suppuration; staphylococcus pyogenes aureus; sarcina lutea.
1571—Lochia, for bacteriologic examination.	Micrococci of suppuration; staphylococcus pyogenes albus; bacilli mycoides	1591—Lochia, for bacteriologic examination.	Micrococci of suppuration; staphylococcus pyogenes albus.
1572—Lochia, for bacteriologic examination.	Micrococci of suppuration; streptococcus pyogenes; staphylococcus pyogenes albus.	1592—Lochia, for bacteriologic examination.	Micrococci of suppuration; staphylococcus pyogenes albus and aureus.
1573—Inoculation from abdominal cavity, to determine character of infection.	Staphylococcus pyogenes albus.	1593—Inoculation from sinus, to determine character of infection.	Staphylococcus pyogenes albus.
1574—Breast, for histologic diagnosis.	Cystic, with beginning carcinoma.	1594—Urine.	Albuminuria.
1575—Lochia, for bacteriologic examination.	Micrococci of suppuration; staphylococcus pyogenes albus.	1595—Blood, for Widal's test.	Positive.
1576—Catgut, for bacteriologic examination.	Sterile.	1596—Urine for tubercle bacilli.	Negative.*
1577—Inoculation from vagina, to determine character of infection.	Bacillus subtilis; staphylococcus pyogenes aureus.	1597—Blood, for Widal's test.	Negative.*
1578—(a) Inoculation. (b) Spreads from arm, to determine character of infection.	(a) Staphylococcus pyogenes albus; staphylococcus pyogenes aureus; sarcina lutea. (b) Micrococci of suppuration.	1598—Tumor from neck, for histologic diagnosis.	Lost in preparation.
1579—Breast, for histologic diagnosis.	Small spindle cell sarcoma.	1599—Breast, for histologic diagnosis.	Papillary cyst adenoma.
1580—Inoculation from vagina, to determine character of infection.	Micrococcus of gonorrhea; staphylococcus pyogenes aureus; bacillus of the colon group.	1600—Inoculation from blood, to determine character of infection.	Sterile.
1581—(a) Inoculation. (b) Spreads from vaginal secretion, to determine character of infection.	(a) Bacillus coli communis; staphylococcus pyogenes aureus. (b) Micrococcus of gonorrhea.	1601—Inoculation from abdominal cavity, to determine character of infection.	Staphylococcus pyogenes albus.
1582—Material from postmortem, for histologic diagnosis.	Traumatic myelitis.	1602—Blood, for Widal's test.	Positive.
1583—Tumor from shoulder, for histologic diagnosis.	Lipoma.	1603—Fallopian tubes, for histologic diagnosis.	Salpingitis.
		1604—Inoculations from cheek to determine character of infection.	Sterile.
		1605—Blood, for Widal's test.	Negative.*
		1606—Gastric contents, for hydrochloric acid.	Positive.
		1607—Gastric contents, for hydrochloric acid.	Positive.
		1608—Material from autopsy, for histologic diagnosis.	Pernicious anemia.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1609—Cervix and tumor, for histologic diagnosis.	Edematous and infected fibromyoma.	1637—Tissue from cervix, for histologic diagnosis.	Squamous epithelioma.
1610—Blood, for Widal's test.	Negative.*	1638—Blood, for Widal's test.	Negative.*
1611—Tumors from neck and in front of parotid gland, for histologic diagnosis.	Large cell alveolar melanotic sarcoma.	1639—Material from penis, for histologic diagnosis.	Chronic phagedena with tuberculosis.
1612—Sputum, for tubercle bacilli.	Negative.*	1640—Blood, for Widal's test.	Positive.
1613—Urine.	Albuminuria.	1641—Blood, for Widal's test.	Positive.
1614—Fallopian tube, for histologic diagnosis.	Granulation tissue as a result of infection.	1642—Inoculation from ankle, to determine character of infection.	Micrococcus pyogenes aureus; bacillus subtilis.
1615—Blood, for Widal's test.	Negative.*	1643—Gastric contents, for hydrochloric acid.	Negative.*
1616—Tissue from uterus, for histologic diagnosis.	Organizing blood clot.	1644—Blood, for Widal's test.	Positive.
1617—Gland from neck, for histologic diagnosis.	Lymphadenitis and perilymphadenitis.	1645—Inoculation from throat, to determine character of infection.	Diplococcus of Sternberg; Bacillus diphtheriz.
1618—Portion of lower jaw, for histologic diagnosis.	Inferior dental neuralgia.	1646—Breast, for histologic diagnosis.	Schirrous carcinoma.
1619—Blood, for Widal's test.	Negative.*	1647—Tissue from nasal ulcer, for histologic diagnosis.	Inflammatory tissue.
1620—Sections of uterus, for histologic diagnosis.	Adenoma.	1648—Testicle, for histologic diagnosis.	Tuberculous epididymitis.
1621—Eye, for histologic diagnosis.	Endothelioma.	1649—Penis, for histologic diagnosis.	Chronic phagedena with tuberculosis.
1622—Tissue from pharyngeal vault, for histologic diagnosis.	Infectious granuloma.	1650—Tissue from forearm, for histologic diagnosis.	Epithelioma.
1623—Tumor of arm, for histologic diagnosis.	Mixed cell sarcoma.	1651—Inoculation from heart, to determine character of infection.	Staphylococci pyogenes albus and aureus.
1624—Infra-orbital nerve, for histologic diagnosis.	Infra-orbital neuralgia.	1652—Brain, for histologic diagnosis.	Syphiloma.
1625—Blood, for Widal's test.	Negative.*	1653—Tissue from lip, for histologic diagnosis.	Specimen lost.
1626—Breast, for histologic diagnosis.	Schirrous carcinoma.	1654—Tissue from lower jaw, for histologic diagnosis.	Follicular odontome.
1627—Ulcer of face, for histologic diagnosis.	Squamous-cell epithelioma.	1655—Blood, for Widal's test.	Positive.
1628—Testicle and vas deferens, for histologic diagnosis.	Interstitial inflammation.	1656—Material from postmortem, for histologic diagnosis.	Fatty degeneration of heart.
1629—Tissue from infected wound, for histologic diagnosis.	Specimen lost.	1657—Gastric contents, for hydrochloric acid.	Positive.
1630—Glands and retained testicle, for histologic diagnosis.	Acute, infective lymphadenitis.	1658—Blood, for Widal's test.	Positive.
1631—Ovary, for histologic diagnosis.	Chronic productive inflammation.	1659—Fecal matter, for bacteriologic examination.	Staphylococcus pyogenes aureus and bacilli of colon group.
1632—Tumor from mouth, for histologic diagnosis.	Papilloma.	1660—Blood, for Widal's test.	Positive.
1633—Testicle, for histologic diagnosis.	Hypoplasia and hyperplasia.	1661—Inoculation, to determine character of infection.	Micrococcus pyogenes aureus; bacillus coli communis.
1634—Spinal cord, for histologic diagnosis.	Locomotor ataxia.	1662—Blood, for Widal's test.	Negative.*
1635—Urine.	Albuminuria.	1663—Blood, for Widal's test.	Negative.*
1636—Inoculation from ascitic fluid to determine character of infection.	Staphylococcus pyogenes albus.	1664—Blood, for Widal's test.	Negative.*
		1665—Brain and cord, for histologic diagnosis.	Tabes.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1666—Blood clot (?) for histologic diagnosis.	Blood clot.	1694—Tissue from bladder, for histologic diagnosis.	Examination not yet completed.
1667—Tissue from liver, for his- tologic diagnosis.	Abscess.	1695—Blood, for Widal's test.	Positive.
1668—Sputum, for tubercle bacilli.	Negative *	1696—Urine, for tubercle bacilli	Negative.*
1669 - Gastric contents, for hydro- chloric acid.	Negative.*	1697—Sputum, for tubercle bac- illi.	Negative.*
1670—(a) Uterus, (b) Ovary for histologic diagnosis.	(a) Fibromyoma. (b) Endothelioma.	1698—Urine.	Negative *
1671—Urine	Negative.*	1699—Tumor from face, for histo- logic diagnosis.	Perithelioma.
1672—Blood, for Widal's test.	Negative.*	1700—Urine.	Pyuria.
1673—Blood, for Widal's test.	Negative.*	1701—Submaxillary gland, for histologic diagnosis.	Chronic inflammation
1674—Gastric contents, for hydro- chloric acid.	Positive.	1702—Tissue from vaginal wall, for histologic diagnosis	Cavernous lymphangioma.
1675—Sebaceous cyst (?) for his- tologic diagnosis.	Fibroma.	1703—Placenta, for histologic diagnosis.	Examination not yet completed
1676—Inoculations from pus, to determine character of in- fection.	Diplococcus of Sternberg; Staphy- lococci pyogenes al- bus and aureus.	1704—Inoculation from throat, to determine character of in- fection.	Micrococcus pyogenes albus; dip- lococcus of Sternberg
1677—Cyst from mouth, for his- tologic diagnosis.	Branchial dermoid.	1705—Tumor from neck, for his- tologic diagnosis	Cavernous hemangioma.
1678—Scrapings from uterus, for histologic diagnosis.	Adeno-carcinoma.	1706—Tumor from rib, for histo- logic diagnosis.	Examination not yet completed.
1679—Urine.	Albuminuria.	1707—Inoculation from vagina, to determine character of infection.	Micrococcus pyogenes albus; Sac- charomycetes albic- ans.
1680—Tissue from inferior max- illa, for histologic diagnosis.	Lymphangio- endothelioma.	1708—Urine.	Pyuria.
1681—Breast, for histologic diag- nosis.	Chronic productive mastitis.	1709—Bone from femur, for his- tologic diagnosis.	Chronic productive osteitis.
1682—Tissue from jaw, for histo- logic diagnosis.	Lupus.	1710—Blood, for Widal's test.	Negative.*
1683—Veins and nerves, for his- tologic diagnosis.	Thrombophlebitis.	1711—Sputum, for tubercle bacilli.	Negative.*
1684—Blood, for Widal's test.	Negative.*	1712—Material from autopsy, for histologic diagnosis.	Puerperal sepsis.
1685—Urine.	Albuminuria.	1713—Blood, for Widal's test.	Negative.*
1686—Tissue from arm, for histo- logic diagnosis	Alveolar mixed cell sarcoma	1714—Blood, for Widal's test.	Negative.*
1687—Urine.	Albuminuria.	1715—Urine.	Albuminuria.
1688—Bacteriology of autopsy findings.	Staphylococcus pyo- genes albus; diplo- coccus pneumoniae.	1716—Blood, for Widal's test.	Negative.*
1689—Tumor from face, for histo- logic diagnosis.	Epithelioma.	1717—Sinus, and fragment of tissue from tibia, for histo- logic diagnosis.	Chronic inflamma- tion of connective tissue.
1690—Tissue from uterus, for his- tologic diagnosis.	Decidual tissue.	1718—Urine.	Pyuria
1691—Material from autopsy, for histologic diagnosis. Inoculations from heart, to determine character of in- fection.	Hydrothorax, pericarditis, etc. Staphylococcus pyogenes albus.	1719—Inoculation from spinal fluid to determine charac- ter of infection.	Micrococci of sup- puration.
1692—Blood, for Widal's test.	Positive.	1720—Blood, for Widal's test.	Negative.*
1693—Spreads from discharge from anus, to determine character of infection.	Micrococci of suppuration.	1721—Section of liver, and tumor under liver, for histologic diagnosis.	Round cell sarcoma.
		1722—Blood, for Widal's test.	Negative.*

The following is a list of specimens and materials examined in the Laboratories during the year 1902 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1723—Lip, for histologic diagnosis.	Squamous cell epithelioma.	1747—Tissue from autopsy, for histologic diagnosis.	Hepatic cirrhosis.
1724—Testicle, for histologic diagnosis.	Ectopia.	1748—Tissue from superior maxilla, for histologic diagnosis.	Specimen unfit for examination.
1725—Fluid from scrotum, for bacteriologic examination.	Negative.*	1749—Sputum, for tubercle bacilli.	Present.
1726—Blood, for Widal's test.	Positive.	1750—Blood, for Widal's test.	Negative.*
1727—Organs from autopsy, for histologic diagnosis.	Carcinosis, primary in stomach.	1751—Inoculation from eye, to determine character of infection.	Bacillus of Axenfeld and Morax.
1728—Glands from groin, for histologic diagnosis.	Tuberculosis.	1752—Inoculation from gum, to determine character of infection.	Streptococcus pyogenes, and Staphylococcus pyogenes aureus.
1729—Testicle, for histologic diagnosis.	Cystic degeneration.	1753—Inoculations, to determine character of infection.	Staphylococcus pyogenes aureus.
1730—Urine.	Albuminuria.	1754—Tonsil, for histologic diagnosis.	Squamous cell epithelioma.
1731—Blood, for Widal's test.	Negative.*	1755—Uterus and appendages, for histologic diagnosis.	Squamous cell epithelioma of cervix.
1732—Sputum, for tubercle bacilli.	Negative.*	1756—Tissue from lower lip, for histologic diagnosis.	Inflammatory tissue.
1733—Blood, for Widal's test.	Negative.*	1757—Blood, for Widal's test.	Positive.
1734—Groin, tissue from, for histologic diagnosis.	Alveolar sarcoma.	1758—Blood, for Widal's test.	Positive.
1735—Blood, for Widal's test.	Negative.*	1759—Mamma, for histologic diagnosis.	Adenocarcinoma.
1736—Ovary, for histologic diagnosis.	Endothelioma with chronic ovarian cirrhosis.	1760—Tissue from tongue, for histologic diagnosis.	Lymphoid tissue.
1737—Lymph glands, for histologic diagnosis.	Chronic tuberculosis.	1761—Undescended testicle, for histologic diagnosis.	Aspermatogenesis.
1738—Mammary glands, for histologic diagnosis.	Cystic degeneration	1762—Spreads and inoculations from vagina, for gonococci.	Negative.*
1739—Inoculation from wound, to determine character of infection.	Staphylococcus pyogenes cereus flavus.	1763—Fluid from chest, for bacteriologic examination.	Staphylococcus pyogenes aureus.
1740—Inoculation from gall bladder, to determine character of infection.	Bacillus coli communis.	1764—Blood, for Widal's test.	Negative.*
1741—Blood, for Widal's test.	Negative.*	1765—Urine.	Albuminuria.
1742—Urine.	Hematuria.	1766—Inoculation from eye, to determine character of infection.	Sterile.
1743—Urine, for lead.	Negative.*	1767—Fluid from abdominal cavity, for bacteriologic examination.	Bacillus coli communis.
1744—Gland from omentum, for histologic diagnosis.	Gastro-hepatic carcinoma.	1768—Right second toe, for histologic diagnosis.	Chronic inflammation.
1745—Portion of tunica vaginalis, for histologic diagnosis.	Inflammatory tissue		
1746—Tonsil, for histologic diagnosis.	Round cell sarcoma.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1769—Tissue from eye-lid, for histologic diagnosis.	Squamous cell epithelioma.	1797—Urine.	Albuminuria.
1770—Inoculation from neck, to determine character of infection.	Tubes not received at the Laboratory.	1798—Fetus	No report requested.
1771—Wall of bursa, for histologic diagnosis.	Chondro-myxofibro-sarcoma	1799—Inoculation from fetus, to determine character of infection.	Staphylococcus pyogenes aureus.
1772—Testicle, for histologic diagnosis.	Tuberculosis.	1800—Uterus, for histologic diagnosis.	Fibromyoma.
1773—Uterine tissue, for histologic diagnosis.	Fibro-myoma.	1801—Blood, for Widal's test.	Positive.
1774—Tissue from thumb, for histologic diagnosis.	Granulation tissue.	1802—Tissue from hand, for histologic diagnosis.	Granulation tissue.
1775—Prepuce, for histologic diagnosis.	Papilloma.	1803—Inoculation from liver abscess, to determine character of infection.	Micrococcus pyogenes aureus.
1776—Uterine tissue, for histologic diagnosis.	Fibro-myoma.	1804—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
1777—Placenta and membranes, for histologic diagnosis.	Endarteritis	1805—Tissue from nose, for histologic diagnosis.	Cavernous hemangioma.
1778—Uterine tissue, for histologic diagnosis.	Necrosing fibrous polyp.	1806—Cervix, for histologic diagnosis.	Tubular adenoma and cylindric-cell carcinoma.
1779—Tissue from eye-lid, for histologic diagnosis.	Endothelioma.	1807—Blood, for Widal's test.	Negative.*
1780—Mamma, for histologic diagnosis.	Cystic degeneration.	1808—Parotid gland, for histologic diagnosis.	Lymphangio-endothelioma.
1781—Inoculation from liver, to determine character of infection.	Sterile.	1809—Blood, for Widal's test.	Negative.*
1782—Blood, for Widal's test.	Negative.*	1810—Uterus, for histologic diagnosis.	Myoma and beginning necrosis.
1783—Sputum, for tubercle bacilli.	Negative.*	1811—Blood, for Widal's test.	Negative.*
1784—Tissue from back, for histologic diagnosis.	Alveolar melanotic sarcoma.	1812—Heart, for histologic diagnosis.	Chronic fibrous myocarditis.
1785—Mamma, for histologic diagnosis.	Scirrhus carcinoma.	1813—Lymph glands, for histologic diagnosis.	Tuberculosis.
1786—Tissue from parotid region, for histologic diagnosis.	Infected.	1814—Inoculation from eye, to determine character of infection.	Sterile.
1787—Mamma, for histologic diagnosis.	Scirrhus carcinoma.	1815—Blood, for Widal's test.	Positive.
1788—Blood, for Widal's test.	Positive.	1816—Inoculation from lung, to determine character of infection.	Sterile.
1789—Uterus, tubes and ovaries, for bacteriologic examination.	Sterile.	1817—Blood, for Widal's test.	Positive.
1790—Tumor from neck, for histologic diagnosis.	Hyperplastic goitre	1818—Blood, for Widal's test.	Negative.*
1791—Blood, for Widal's test.	Positive.	1819—Inoculation from spinal cord, to determine character of infection.	Negative.*
1792—Blood, for Widal's test.	Negative.*	1820—Blood, for Widal's test.	Positive.
1793—Gastric contents, for lactic acid.	Present.	1821—Blood, for Widal's test.	Positive.
1794—Mamma, for histologic diagnosis.	Scirrhus carcinoma.	1822—Blood, for Widal's test.	Negative.*
1795—Blood, for Widal's test.	Negative.*	1823—Tissue from cheek, for histologic diagnosis.	Squamous-cell epithelioma.
1796—Tissue from roof of mouth, for histologic diagnosis.	Lymphangio-endothelioma.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1824—Blood, for Widal's test.	Positive.	1851—Jaw, for histologic diagnosis.	Mixed-cell sarcoma.
1825—Blood, for Widal's test.	Positive.	1852—Great trochanter, for histologic diagnosis.	Alveolar mixed-cell sarcoma.
1826—Blood, for Widal's test.	Positive.	1853—Placental tissue, to determine if malignant.	Not malignant.
1827—Tissue from forehead, for histologic diagnosis.	Squamous-cell epithelioma.	1854—Blood, for Widal's test.	Negative.*
1828—Blood, for malaria.	Negative *	1855—Inoculation from hand, for B. tetani.	Negative.*
1829—Blood, for Widal's test.	Negative.*	1856—Blood, for Widal's test.	Negative *
1830—Blood, for Widal's test.	Positive.	1857—Blood, for Widal's test.	Positive.
1831—Eye, for histologic diagnosis.	Lymphangio- and hemangio-perithelioma.	1858—Blood, for Widal's test.	Negative.*
1832—Urine.	Negative *	1859—Jaw, for histologic diagnosis.	Squamous-cell epithelioma.
1833—Sputum, for tubercle bacilli.	Present.	1860—Jaw, for histologic diagnosis.	Chondro-sarcoma.
1834—Blood, for Widal's test.	Positive.	1861—Pus from joint, for bacteriologic examination.	Tubercle bacilli.
1835—Blood, for Widal's test.	Negative.*	1862—Mamma, for histologic diagnosis.	Fibroma.
1836—Blood, for Widal's test.	Negative *	1863—Inoculation from eye, to determine character of infection.	Bacillus coli communis.
1837—Mamma, for histologic diagnosis.	Intra- and pericanalicular fibroma.	1864—Urine.	Albuminuria.
1838—Mamma, for histologic diagnosis.	Scirrhus carcinoma.	1865—Portion of tongue, for histologic diagnosis.	Squamous epithelioma.
1839—Inoculation from abscess, to determine character of infection.	Staphylococcus pyogenes aureus.	1866—Blood, for Widal's test.	Negative.*
1840—Mamma, for histologic diagnosis.	Scirrhus carcinoma.	1867—Urine, for bacteriologic examination.	Negative.*
1841—Tissue for knee, for histologic diagnosis.	Ulcerating squamous-cell epithelioma.	1868—Tissue from kidney, for histologic diagnosis.	Round cell sarcoma.
1842—Foot, for histologic diagnosis.	Chondro-myxo-fibro-sarcoma.	1869—Blood, for Widal's test.	Negative.*
1843—Mass from leg, for histologic diagnosis.	Negative.*	1870—Thoracic fluid, for bacteriologic examination.	Sterile.
1844—Inoculation from peritoneum, to determine character of infection.	Negative.*	1871—Tissue from leg, for histologic diagnosis.	Granulation tissue.
1845—Tissue from abdomen, for histologic diagnosis.	Tubercular peritonitis.	1872—Blood, for Widal's test.	Negative.*
1846—Salivary gland, for histologic diagnosis.	Subacute interstitial productive inflammation.	1873—Tissue from liver, for histologic diagnosis.	Necrosis.
1847—Glands from neck, for histologic diagnosis.	Tuberculous and suppurative lymphadenitis and perilymphadenitis.	1874—Blood, for Widal's test.	Negative.*
1848—Anus, for histologic diagnosis.	Granulation tissue.	1875—Orbit, for histologic diagnosis.	Lymphangio-endothelioma.
1849—Blood, for Widal's test.	Negative.*	1876—Pus from eye for bacteriologic examination.	Staphylococcus pyogenes aureus.
1850—Blood, for Widal's test.	Negative.*	1877—Blood, for Widal's test.	Negative.*
		1878—Blood, for Widal's test.	Negative.*
		1879—Inoculation from liver abscess, to determine character of infection.	Sterile.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1880—Mamma, for histologic diagnosis.	Chronic productive mastitis with cystic degeneration.	1909—Nerve, for histologic diagnosis.	Fibroneuroma.
1881—Leg, for histologic diagnosis.	Squamous cell epithelioma.	1910—Blood, for Widal's test.	Negative.*
1882—Blood, for Widal's test.	Negative.*	1911—Blood, for Widal's test.	Negative.*
1883—Blood, for Widal's test.	Negative.*	1912—Testicle and appendages, for histologic diagnosis.	Suppurative orchitis.
1884—Inguinal hernia, for histologic diagnosis.	Negative.*	1913—Mamma, for histologic diagnosis.	Fibroadenoma.
1885—Fluid from abdomen, for bacteriologic examination.	Tubercle bacilli.	1914—Subphrenic abscess, for histologic diagnosis.	Fibroadenoma.
1886—Urine.	Albuminuria.	1915—Inoculations, to determine character of infection.	Sterile.
1887—Blood, for malaria.	Present.	1916—Blood, for Widal's test.	Negative.*
1888—Urine.	Albuminuria.	1917—Inoculation from leg, to determine character of infection.	Sterile.
1889—Blood, for Widal's test.	Negative.*	1918—Tissue from jaw, for histologic diagnosis.	Squamous cell epithelioma.
1890—Urine, for diazo reaction.	Positive.	1919—Uterine tumor, for histologic diagnosis.	Fibroma undergoing necrosis.
1891—Urine.	Negative.*	1920—(a) Urine; (b) Sputum, for tubercle bacilli.	(a) Oxaluria. (b) Negative.*
1892—Fluid from abdomen, for bacteriologic examination.	Tubercle bacilli.	1921—Tissue from anus, for histologic diagnosis.	Granulation tissue.
1893—Blood, for Widal's test.	Negative.	1922—Tissue from head, for histologic diagnosis.	Squamous cell epithelioma.
1894—Inoculation from knee, to determine character of infection.	Sterile.	1923—Tissue from neck, for histologic diagnosis.	Secondary carcinoma.
1895—Blood, for Widal's test.	Negative.*	1924—Ovary, for histologic diagnosis.	Papillary cystadenoma.
1896—Blood, for Widal's test.	Negative.*	1925—Blood count.	Anemia.
1897—Blood, for Widal's test.	Negative.*	1926—Blood for Widal's test.	Positive.
1898—Sputum, for tubercle bacilli.	Negative.*	1927—Blood, for Widal's test.	Positive.
1899—Blood, for Widal's test.	Positive.	1928—Pleural effusion, for bacteriologic examination.	Negative.*
1900—Blood, for Widal's test.	Negative.*	1929—Sputum, for tubercle bacilli.	Negative.*
1901—Inoculation from cheek, to determine character of infection.	Sterile.	1930—Concretion and tissue from appendix, for histologic examination.	Subacute peritonitis.
1902—Tissue from head for histologic diagnosis.	Squamous epithelioma.	1931—Blood, for Widal's test.	Positive.
1903—Blood, for Widal's test.	Negative.*	1932—Pleural effusion, for bacteriologic examination.	Negative.*
1904—Tissue from rectum, for histologic diagnosis.	Adenocarcinoma.	1933—Eye, for bacteriologic examination.	Pure culture pneumococcus.
1905—Blood, for Widal's test.	Positive.	1934—Fluid from groin, for bacteriologic examination.	Sterile.
1906—Blood, for Widal's test.	Positive.	1935—Inoculation from sacrum, to determine character of infection.	Bacillus coli communis.
1907—Blood, for Widal's test.	Positive.	1936—Mamma, for histologic examination.	Scirrhus with beginning suppuration.
1908—Milk, for bacteriologic examination.	Bacillus coli communis.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1937—Blood, for Widal's test.	Positive.	1963—Blood, for Widal's test.	Negative.*
1938—Blood, for Widal's test	Positive.	1964—Tumor of neck, for histo- logic diagnosis.	Squamous-cell epi- thelioma under- going necrosis.
1939—Blood, for Widal's test.	Positive.	1965—Portion of nerve, for histo- logic diagnosis.	Chronic interstitial neuritis.
1940—Blood, for Widal's test.	Positive.	1966—Material from gall bladder, for bacteriologic examina- tion.	Sterile
1941—(a) Heart; (b) Liver; (c) Kidney, for histologic diagnosis.	(a) Fatty infiltration; fibrous myocarditis. (b) Red atrophy, fatty infiltration. (c) Chronic diffuse nephritis.	1967—Tissue from tongue, for his- tologic diagnosis.	Squamous cell epithelioma.
1942—Blood, for Widal's test.	Negative.*	1968—Glands from neck, for his- tologic diagnosis.	Small round-cell sarcoma.
1943—(a) Blood count; (b) Spu- tum, for tubercle bacilli.	(a) Negative * (b) Negative.*	1969—Tissue from jaw, for histo- logic diagnosis.	Fibro-sarcoma.
1944—Blood count.	Negative.*	1970—Bacteriologic examination of inoculations from Prof. Keen's clinic.	Tabulated report submitted to date.
1945—Inoculation from leg, to determine character of in- fection.	Micrococcus of sup- puration and micro- coccus pyogenes albus.	1971—Blood, for Widal's test.	Positive.
1946—Urine, for bacteriologic ex- amination.	Bacillus coli communis.	1972—Anus, for histologic diag- nosis.	Lymphangio- endothelioma.
1947—Urine.	Negative.*	1973—Blood, for Widal's test.	Positive.
1948—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	1974—Inoculation from perine- phritic abscess, to deter- mine character of infection.	Micrococcus pyogenes aureus
1949—Inoculation from eye, to determine character of in- fection.	Staphylococci pyo- genes albus and aureus.	1975—Pleural effusion, for bac- teriologic examination.	Sterile.
1950—Blood, for Widal's test.	Positive.	1976—Inoculation from abdom- inal cavity, to determine character of infection	Bacillus coli communis.
1951—Inoculation from gall blad- der, to determine character of infection.	Sterile.	1977—Mamma, for histologic diagnosis.	Fibro-adenoma.
1952—Tissue from rectum, for histologic diagnosis	Adenocarcinoma.	1978—Blood, for Widal's test.	Negative.*
1953—Blood, for Widal's test.	Positive.	1979—Tissue from cervix, for his- tologic diagnosis	Spheroidal-cell carcinoma.
1954—Silver catgut, for bacterio- logic examination.	Sterile.	1980—Blood, for Widal's test.	Positive.
1955—Inoculation, to determine character of infection	Staphylococcus pyogenes aureus.	1981—Blood, for Widal's test.	Positive.
1956—Rectum, for histologic diag- nosis.	Cylindric-cell carci- noma undergoing necrosis.	1982—Urine.	Bacteriuria.
1957—Mamma, for histologic diagnosis	Papillary adeno- cystoma.	1983—Fluid from ovarian cyst, for cytologic diagnosis.	Cytologic report submitted.
1958—Urine.	Pyuria.	1984—Pus from parotid gland, for bacteriologic examination.	Staphylococcus pyogenes aureus.
1959—Tissue from arm, for histo- logic diagnosis.	Myxosarcoma.	1985—Larynx, for histologic diag- nosis.	Epithelioma.
1960—Larvae from bladder, for diagnosis.	H. canicularis.	1986—Inoculation from sarcoma, to determine character of infection.	Bacillus coli com- munis; Saccharo- myces albicans.
1961—Tumor of nasopharynx, for histologic diagnosis.	Small round-cell sarcoma.	1987—Blood count.	Negative.*
1962—Material from rectum, for bacteriologic examination.	Bacillus coli communis.	1988—Inoculation from blood, to determine character of in- fection.	Sterile.
		1989—Blood, for Widal's test.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
1990—Blood, for Widal's test.	Positive.	2016—Blood, for Widal's test.	Negative.*
1991—Blood, for Widal's test.	Negative.*	2017—Tissue from stomach, for histologic diagnosis	Encephaloid carcinoma.
1992—Blood, for Widal's test.	Positive.	2018—Tissue from knee-joint, for histologic diagnosis	Caseous tuberculosis.
1993—Inoculation from pleural cavity, to determine char- acter of infection.	Streptococcus pyo- genes and staphylo- coccus pyogenes aureus.	2019—Blood, for Widal's test.	Positive.
1994—Blood, for Widal's test.	Positive.	2020—Blood, for Widal's test.	Positive.
1995—Tissue from nerve, for his- tologic diagnosis.	Chronic interstitial and parenchyma- tous neuritis.	2021—(a) Mamma, (b) axillary glands, for histologic diag- nosis.	(a) Cystic involution; chronic interstitial mastitis. (b) Lymphadenitis.
1996—Blood, for Widal's test.	Positive.	2022—Glands from neck, for his- tologic diagnosis.	Lymphangio- endothelioma.
1997—Growth from nostril, for histologic diagnosis.	Hemangio-cysta- dendo-myxofibroma.	2023—Nerve from ulna, for histo- logic diagnosis.	Neuritis.
1998—Mamma, for histologic diagnosis.	Papillary cystadenoma.	2024—Blood, for Widal's test.	Negative.*
1999—Tissue from lip, for histo- logic diagnosis.	Squamous epitheli- oma with beginning metastases in lymph-node.	2025—Mamma, for histologic diagnosis.	Chronic productive interstitial mastitis with cystic degener- ation.
2000—Inoculation from abscess, to determine character of infection.	Sterile.	2026—Blood, for Widal's test.	Positive.
2001—Thyroid gland, for histo- logic diagnosis.	Papillary cystadeno- ma undergoing car- cinomatous trans- formation.	2027—Tumor from neck, for his- tologic diagnosis	Branchial cyst show- ing pyogenic infec- tion.
2002—Tumor from sacral region, for histologic diagnosis.	Sacrococcygeal cyst.	2028—Urine.	Bacteriuria.
2003—Blood for Widal's test.	Negative.*	2029—Vocal cords, for histologic diagnosis.	Squamous cell epithelioma.
2004—Cheek, for histologic diag- nosis.	Squamous-cell epithelioma.	2030—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
2005—Blood, for Widal's test.	Negative.*	2031—Blood, for Widal's test.	Negative.*
2006—Blood, for Widal's test.	Positive.	2032—Appendix, for histologic diagnosis.	Catarrhal and inter- stitial appendicitis.
2007—Blood, for Widal's test.	Positive.	2033—Mamma and glands from axilla, for histologic diag- nosis.	Alveolar sarcoma.
2008—Portion of omentum, for histologic diagnosis.	Adipose tissue show- ing slight inflamma- tion.	2034—Inoculation from cellulitis, to determine character of infection	Bacillus coli communis.
2009—Section of kidney, for his- tologic diagnosis.	Chronic diffuse inflammation.	2035—Umbilicus, for histologic diagnosis.	Alveolar sarcoma showing slight mela- nosis.
2010—Tissue from eyelid, for his- tologic diagnosis.	Squamous-cell epithelioma.	2036—Tumor from antrum, con- taining eye, for histologic diagnosis.	Squamous cell epithelioma.
2011—Glands from neck, for his- tologic diagnosis.	Acute tubercular lymphadenitis.	2037—Blood, for Widal's test.	Positive.
2012—Tissue from face, for histo- logic diagnosis.	Squamous-cell epithelioma.	2038—Blood, for Widal's test.	Positive.
2013—Tissue from buttock, for histologic diagnosis.	Cylindric-cell carci- noma; productive interstitial myositis.	2039—Tumor from mamma, for histologic diagnosis.	Pericanalicular myxofibroma.
2014—Tissue from rectum, for histologic diagnosis.	Inflammatory tissue.	2040—Blood, for Widal's test.	Positive.
2015—Blood, for bacteriologic ex- amination.	Staphylococcus pyo- genes albus; sarcina.	2041—Supra-orbital nerve, for his- tologic diagnosis.	Neuritis.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2042—Tissue from knee-joint, for histologic diagnosis.	Tuberculosis involv- ing articular carti- lage and adjacent bone.	2047—Urine.	Hematuria.
2043—Foreskin, for histologic di- agnosis.	Squamous cell epithelioma.	2048—Blood, for Widal's test.	Negative.*
2044—Blood, for Widal's test.	Negative.*	2049—Inoculation from ulcer, to determine character of in- fection.	Staphylococci pyo- genes aureus, and cereus albus.
2045—Tumor from toe, for histo- logic diagnosis.	Alveolar spheroidal cell sarcoma.	2050—Tissue from ulcer, for his- tologic diagnosis.	Tuberculosis.
2046—Blood, for Widal's test.	Negative.*	2051—Blood, for Widal's test.	Negative.*

LABORATORIES.

The following is a report of the work done in the laboratories of the Jefferson Medical College Hospital for the year ending December 31st, 1903. The total number of detailed reports submitted during the year is 509, an increase of fifty-five per cent. over the number for the corresponding period of 1902. The reports are numbered consecutively, the numbers corresponding with the filed copies in the laboratory records. This record of over 2500 examinations compiled from the laboratory files constitutes a fair index of the value of laboratory records and may be consulted to advantage by those desiring statistical facts, particularly with regard to the relative frequency of tumors, the organs involved, and similar data. Incidentally they show, as well as figures can, the scope of the work done in a fairly busy clinical laboratory.

The summary of the laboratory record is followed by tables of the separately indexed reports of the reports of the urine, sputum, gastric-contents and blood examinations, for the compilation of which I am indebted to Dr. Thomas C. Stellwagen, Jr., Resident Pathologist.

The following is a list of specimens and materials examined in the Laboratories during the year 1903 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2052—Blood, for Widal's test.	Positive.	2074—Blood, for Widal's test.	Positive.
2053—Tissue from leg, for histologic diagnosis.	Spheroidal-cell sarcoma.	2075—Blood, for Widal's test.	Negative.*
2054—Mamma and axillary glands, for histologic diagnosis.	Scirrhus carcinoma.	2076—Blood, for Widal's test.	Positive.
2055—Section of spinal accessory nerve, for histologic diagnosis.	Chronic interstitial and parenchymatous neuritis.	2077—Gauze saturated with pus from appendix, to determine character of infection.	Staphylococcus pyogenes aureus.
2056—Mamma, for histologic diagnosis.	Scirrhus carcinoma.	2078—Inoculation from leg, to determine character of infection.	Pneumococcus.
2057—Blood, for Widal's test.	Positive.	2079—Urine, for bacteriologic examination.	Bacillus coli communis and Staphylococcus pyogenes citreus.
2058—Blood, for Widal's test.	Negative.*	2080—Blood, for Widal's test.	Negative.*
2059—Blood, for Widal's test.	Negative.*	2081—Blood, for Widal's test.	Negative.*
2060—Blood, for Widal's test.	Negative.*	2082—Blood, for Widal's test.	Negative.*
2061—Inoculation from tonsil, to determine character of infection.	Pneumococcus, and Staphylococcus pyogenes albus.	2083—Tissue from knee-joint, for histologic diagnosis.	Tuberculous arthritis.
2062—Inoculation from thigh, to determine character of infection.	Bacillus tuberculosis and Staphylococcus pyogenes aureus.	2084—Blood, for Widal's test.	Negative.*
2063—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	2085—Blood, for Widal's test.	Positive.
2064—Inoculation from pus, to determine character of infection.	Pneumococcus, and Bacillus coli communis.	2086—Blood, for Widal's test.	Positive.
2065—Blood, for Widal's test.	Positive.	2087—Blood, for Widal's test.	Positive.
2066—Tumor from arm, for histologic diagnosis.	Granulation tissue.	2088—Blood, for Widal's test.	Negative.*
2067—Inoculation from throat, to determine character of infection.	Staphylococcus pyogenes albus.	2089—Inoculation from wrist-joint, to determine character of infection.	Gonococcus and Staphylococcus pyogenes albus.
2068—Cyst, for histologic diagnosis.	Retention cyst.	2090—Blood, for Widal's test.	Positive.
2069—Blood, for Widal's test.	Positive.	2091—Inoculation from appendix, to determine character of infection.	Bacillus coli communis and Pneumococcus.
2070—Tumor from scrotum, for histologic diagnosis.	Infected squamous-cell epithelioma.	2092—Tumor from neck, for histologic diagnosis.	Perithelioma of carotid gland.
2071—Tissue from uterus, for bacteriologic diagnosis.	Cocci of suppuration.	2093—Blood, for Widal's test.	Negative.*
2072—Tumor from scrotum, for histologic diagnosis.	(a) Squamous cell epithelioma. (b) Sebaceous cyst.	2094—Blood, for Widal's test.	Positive.
2073—(a) Tissue from knee-joint, for histologic diagnosis. (b) Inoculation to determine character of infection.	(a) Tuberculosis. (b) Negative.*	2095—Tissue from cervix, for histologic diagnosis.	Cylindric-cell carcinoma.
		2096—Tissue from sacral region, for histologic diagnosis.	Inflammatory new formation.
		2097—Blood, for Widal's test.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2098—Blood, for Widal's test.	Negative.*	2124—Blood, for Widal's test.	Negative.*
2099—Blood, for Widal's test.	Negative.*	2125—Blood, for Widal's test.	Positive.
2100—Inoculation from wrist-joint, to determine character of infection.	Sterile.	2126—M a m m a, for histologic diagnosis.	Chronic productive mastitis.
2101—M a m m a, for histologic diagnosis.	Scirrhus carcinoma.	2127—Blood, for Widal's test.	Positive.
2102—Blood, for Widal's test.	Negative.*	2128—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
2103—Blood, for Widal's test.	Negative.*	2129—Tumors from breasts, for histologic diagnosis.	Peri- and intracanalicular fibroma.
2104—M a m m a and axillary glands, for histologic diagnosis.	Scirrhus carcinoma.	2130—Blood, for Widal's test.	Negative.*
2105—Portion of vastus externus muscle, for histologic diagnosis.	Slight interstitial myositis.	2131—(a) Spreads; (b) Inoculation from abscess of leg, to determine character of infection.	(a) Micrococci of suppuration; (b) Staphylococcus pyogenes aureus.
2106—Blood, for Widal's test.	Negative.*	2132—Blood, for Widal's test.	Positive.
2107—(a) Urine. (b) Blood.	(a) Albuminuria. (b) Anemia.	2133—Fluid from breasts, for bacteriologic examination.	Negative.*
2108—Blood, for bacteriologic examination.	Bacillus pyocyaneus	2134—Breast, for histologic diagnosis.	Cystic adenoma.
2109—Larynx, for histologic diagnosis.	Squamous-cell epithelioma.	2135—Organs from autopsy, for histologic diagnosis.	Septic pneumonia.
2110—M a m m a, for histologic diagnosis.	Chronic productive mastitis, intracanalicular fibroma.	2136—Inoculation from vaginal discharge, to determine character of infection.	Streptococcus pyogenes and Staphylococcus pyogenes albus.
2111—Material washed from bowel, for histologic diagnosis.	Pseudomembrane.	2137—Tumor from neck, for histologic diagnosis.	Tuberculous lymphadenitis
2112—M a m m a, for histologic diagnosis.	Cystic fibroadenoma.	2138—Tissue from leg, for histologic diagnosis.	Melanotic, mixed-cell sarcoma of skin.
2113—M a m m a, for histologic diagnosis.	Hemangio-endothelioma.	2139—Brain, for histologic diagnosis.	Examination not completed.
2114—Cyst from sacral region, for histologic diagnosis.	Dermoid cyst.	2140—Urine.	Negative.*
2115—Inoculation from neck, to determine character of infection.	Staphylococcus pyogenes aureus.	2141—Blood, for Widal's test.	Positive.
2116—Tissue from tongue, for histologic diagnosis.	Infected ulcer.	2142—Inoculation from perirenal abscess, to determine character of infection.	Bacillus pyogenes foetidus.
2117—Tissue from rib, for histologic diagnosis.	Chronic interstitial myositis, osteomyelitis.	2143—Tumor from parotid gland, for histologic diagnosis.	Specimen lost.
2118—Inoculations from rib, to determine character of infection.	Bacillus typhosus.	2144—Inoculations from blood, to determine character of infection.	Sterile.
2119—Inoculations from peritoneal fluid, to determine character of infection.	Bacillus coli communis.	2145—Blood, for Widal's test.	Negative.*
2120—Tissue from eye-brow, for histologic diagnosis.	Alveolar sarcoma, mixed-cell, round predominating.	2146—Blood, for Widal's test.	Negative.*
2121—Inoculations from organs post-mortem, to determine character of infection.	Micrococcus pyogenes citreus, and pneumococcus.	2147—Growth from lower lip, for histologic diagnosis.	Squamous-cell epithelioma.
2122—Tumor of parotid gland, for histologic diagnosis.	Myxo-sarcoma.	2148—Leg, for histologic diagnosis.	Endothelioma.
2123—Inoculation from finger, to determine character of infection.	Staphylococcus pyogenes albus and Bacillus of Friedlander.	2149—Nipple, for histologic diagnosis.	Mammalitis.
		2150—Blood, for Widal's test.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2151—Blood, for Widal's test.	Negative.*	2180—Inoculation from neck, to determine character of in- fection.	Sterile.
2152—Blood, for Widal's test.	Positive.	2181—Material from neck for bac- teriologic examination.	Negative *
2153—Blood, for Widal's test.	Positive.	2182—Tumor from parotid gland, for histologic diagnosis.	Myxo-sarcoma.
2154—Submaxillary gland, for his- tologic diagnosis.	Inflammatory tissue.	2183—Blood, for Widal's test.	Positive.
2155—Mamma, for histologic di- agnosis.	Scirrhus carcinoma.	2184—Spread from abscess of knee, for tubercle bacilli	Negative.*
2156—Capsule of kidney, for his- tologic diagnosis.	Negative.*	2185—Gland from axilla, for histologic diagnosis.	Tuberculous lymphadenitis.
2157—Tumor of ovarian tube, for histologic diagnosis.	Decidual membrane.	2186—Tumor from neck, for histologic diagnosis.	Endothelioma.
2158—Polyp of nose, for histo- logic diagnosis.	Fibroma.	2187—Tumor of thyroid gland, for histologic diagnosis.	Parenchymatous goitre.
2159—Tissue from femur, for his- tologic diagnosis.	Osteomyelitis.	2188—M a m m a, for histologic diagnosis.	Chronic productive interstitial mastitis.
2160—Inoculations from femur, to determine character of in- fection.	Sterile.	2189—Blood, for Widal's test.	Positive.
2161—Blood, for Widal's test.	Negative.*	2190—Blood, for Widal's test.	Positive.
2162—Blood, for Widal's test.	Positive.	2191—Blood, for Widal's test.	Negative.*
2163—Blood count.	Anemia.	2192—Blood, for Widal's test.	Positive.
2164—Blood, for Widal's test.	Positive.	2193—Tumor from sacrum, for histologic diagnosis.	Infected dermoid cyst.
2165—Urine.	Albuminuria.	2194—Tumor of thyroid gland for histologic diagnosis.	Parenchymatous goitre.
2166—Gland from neck, for histo- logic diagnosis.	Slight fibrous hyper- plasia and infection.	2195—Inoculation from appen- dix, to determine character of infection.	Bacillus coli communis.
2167—Blood, for Widal's test.	Positive.	2196—Tissue from lip, for histo- logic diagnosis.	Inflamed mucus gland.
2168—Blood, for Widal's test.	Positive.	2197—Tissue from cervix uteri, for histologic diagnosis.	Adenomatous cysts.
2169—Tissue from neck, for histo- logic diagnosis.	Squamous-cell epithelioma.	2198—Tissue from uterus, for histologic diagnosis.	Glandular endometritis.
2170—Uterine polyp, for histo- logic diagnosis.	Fibro-myoma containing glandular elements.	2199—Inoculation from fibula, to determine character of in- fection.	Staphylococcus pyogenes aureus.
2171—Scrapings from uterus, for histologic diagnosis.	Negative.*	2200—Bone from fibula, for histo- logic diagnosis.	Chronic productive osteitis.
2172—Blood count.	Anemia.	2201—Inoculations from leg, to determine character of in- fection.	Streptococcus pyo- genes; Micrococcus pyogenes albus, and pneumococcus.
2173—Blood, for Widal's test.	Negative.*	2202—Inoculation from hip, to determine character of in- fection.	Staphylococcus pyogenes aureus.
2174—Cerebro-spinal fluid, for bacteriologic examination.	Negative *	2203—Fluid from knee, for bac- teriologic examination.	Synovitis.
2175—Tongue and adjacent tis- sue, for histologic diagno- sis.	Squamous-cell epithelioma, no metastasis.	2204—Ulcer from arm, for histo- logic diagnosis.	Squamous-cell epithelioma.
2176—Blood, for Widal's test.	Positive.	2205—Inoculation from gall- bladder, to determine char- acter of infection.	Micrococcus pyogenes albus.
2177—Mamma, for histologic diagnosis.	Scirrhus carcinoma.		
2178—Appendix, for histologic di- agnosis.	Chronic interstitial and ulcerative appendicitis.		
2179—Inoculation from appendix, to determine character of infection.	Sterile.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2206—Mamma and axillary glands, for histologic diagnosis.	Scirrhus carcinoma.	2226—Tumor from arm, for histologic diagnosis.	Mixed-cell sarcoma.
2207—Blood, for Widal's test.	Positive.	2227—Inoculation from brain, to determine character of infection.	Staphylococcus pyogenes albus.
2208—Blood, for Widal's test.	Positive.	2228—Gland from meso-appendix, for histologic diagnosis.	Beginning sclerosis.
2209—Organs from autopsy, for histologic diagnosis.	Congestion of liver; subacute parenchymatous nephritis; emphysema and hypostatic pneumonia; suppurative peritonitis; ulcerative cholecystitis.	2229—Tissue from forearm, for histologic diagnosis.	Normal striped muscle.
2210—Uterus and ovaries, for histologic diagnosis.	Oöphoritis; papillary cystadenoma.	2230—Glands from neck, for histologic diagnosis.	Chronic caseous tuberculous lymphadenitis.
2211—Gland from stomach, for histologic diagnosis.	Cylindric-cell carcinoma.	2231—Blood, for Widal's test.	Negative.*
2212—Tumor from forehead, for histologic diagnosis.	Squamous-cell epithelioma.	2232—Blood, for Widal's test.	Positive.
2213—Organs from autopsy, for histologic diagnosis.	Apneumotosis; hemorrhagic infiltration of spleen; cloudy swelling of adrenal, liver and kidney.	2233—Blood, for Widal's test.	Positive.
2214—(a) Kidneys, (b) prostate gland, (c) bladder wall, obtained post-mortem for histologic diagnosis.	(a) Chronic, diffuse nephritis. (b) Multiple abscess. (c) Scirrhus carcinoma.	2234—Inoculations from autopsy, to determine character of infection.	Sterile.
2215—Tissue from chin, for histologic diagnosis.	Squamous-cell carcinoma.	2235—Breast, for histologic diagnosis.	Scirrhus carcinoma with metastasis to lymph-nodes.
2216—Appendix, for histologic diagnosis.	Acute ulcerative appendicitis.	2236—Breast, for histologic diagnosis.	Scirrhus carcinoma with metastasis to lymph-nodes.
2217—Inoculation from hernia, to determine character of infection.	Sterile.	2237—Tumor from eyelid, for histologic diagnosis.	Papilloma undergoing epitheliomatous transformation.
2218—Inoculations from thoracic abscess, to determine character of infection.	Bacillus pneumoniae (Friedländer). Staphylococcus pyogenes albus.	2238—(a) Tumor from jaw. (b) section of inferior dental nerve, for histologic diagnosis.	(a) Osteo-chondromixed-cell sarcoma. (b) Chronic interstitial and parenchymatous inflammation.
2219—Inoculation from tibia, to determine character of infection.	Bacillus coli communis.	2239—Inoculation from jaw, to determine character of infection.	Sterile.
2220—Bone from tibia, for histologic diagnosis.	Chronic osteomyelitis.	2240—Tissue from autopsy.	Congenital dislocation of hip, etc.
2221—Inoculation from ankle, to determine character of infection.	Sterile.	2241—Tissue from lip, for histologic diagnosis.	Squamous-cell epithelioma.
2222—Ovarian cyst, for histologic diagnosis.	Adeno-carcinoma.	2242—Scrapings from uterus, for histologic diagnosis.	Glandular carcinoma.
2223—(a) Heart. (b) liver. (c) kidney, (d) pancreas obtained postmortem for histologic diagnosis.	(a) Fatty infiltration and degeneration. (b) Congestion and fatty infiltration; (c) chronic diffuse nephritis. (d) Chronic interstitial pancreatitis.	2243—Placenta and membranes, for histologic diagnosis.	Negative.*
2224—Mamma, for histologic diagnosis.	Scirrhus carcinoma	2244—Tumor from fistula, for histologic diagnosis.	Chronic inflammation.
2225—Inoculation from peritoneal cavity, to determine character of infection.	Micrococci of supuration. Staphylococcus pyogenes citreus.	2245—Eyeball, for histologic diagnosis.	Intraocular hemorrhage.
		2246—Kidney, for macroscopic study.	Hydronephrosis.
		2247—Tissue from knee-joint, for histologic diagnosis.	Chronic productive inflammation.
		2248—Breast, for histologic diagnosis.	Chronic diffuse mastitis.
		2249—Blood, for Widal's test.	Positive.
		2250—Blood, for Widal's test.	Positive.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION	RESULTS.
2251—(a) Bone from inside; (b) bone from outside of tibia, for histologic diagnosis.	(a) Chronic osteomyelitis. (b) Chronic osteomyelitis with osseous hyperplasia.	2275—Blood, for Widal's test.	Positive.
2252—Inoculation from bone, to determine character of infection.	Staphylococcus pyogenes albus.	2276—Blood, for Widal's test.	Negative.*
2253—Spreads made from face, to determine character of infection.	Staphylococci(?)	2277—Inoculations from neck, to determine character of infection.	Bacillus tuberculosis, and Staphylococcus pyogenes aureus and albus.
2254—Glands from neck, for histologic diagnosis.	Chronic caseous tuberculous lymphadenitis.	2278—Tumor from face, for histologic diagnosis.	Mixed-cell sarcoma.
2255—Inoculation from neck, to determine character of infection.	Sterile.	2279—Tissue from cervix, for histologic diagnosis.	Hyperplasia of cervix; glandular endometritis.
2256—Biliary calculi, for diagnosis.	Cholesterin.	2280—Blood, for Widal's test.	Negative.*
2257—Inoculation from gall bladder, to determine character of infection.	Staphylococcus pyogenes albus, and Bacillus coli communis.	2281—M a m m a, for histologic diagnosis.	Scirrhus carcinoma with metastasis to lymph-nodes.
2258—Blood, for Widal's test.	Negative.*	2282—Tumor from mouth, for histologic diagnosis.	Giant-cell sarcoma.
2259—Blood, for Widal's test.	Negative.*	2283—Fluid from abdomen, for bacteriologic examination.	Negative.*
2260—Inoculation from hand, to determine character of infection.	Staphylococcus cereus albus.	2284—Blood, for Widal's test.	Positive.
2261—Submaxillary lymph gland, for histologic diagnosis.	Chronic caseous tuberculous lymphadenitis.	2285—Blood, for Widal's test.	Positive.
2262—Inoculation from submaxillary lymph gland to determine character of infection.	Sterile.	2286—Blood, for Widal's test.	Positive.
2263—Sputum, for tubercle bacilli.	Present.	2287—Blood, for Widal's test.	Positive.
2264—Pile, for histologic diagnosis.	Inflammatory tissue.	2288—Appendix, for histologic diagnosis.	Suppurative inflammation.
2265—Blood, for Widal's test.	Positive.	2289—Fluid from abdomen, for bacteriologic examination.	Staphylococcus pyogenes aureus.
2266—Blood, for Widal's test.	Negative.*	2290—Inoculation from lumbar abscess, to determine character of infection.	Staphylococcus pyogenes aureus.
2267—Fluid from pleural cavity, for tubercle bacilli.	Negative.*	2291—Inoculation from back, to determine character of infection.	Bacillus coli communis, Micrococcus of suppuration.
2268—Nodules from peritoneum, for histologic diagnosis.	Cylindric-cell carcinoma.	2292—Tissue from uterus, for histologic diagnosis.	Glandular endometritis.
2269—Appendix, for histologic diagnosis.	Acute suppurative appendicitis.	2293—M a m m a, for histologic diagnosis.	Chronic productive interstitial mastitis; cystic involution.
2270—Tissue from ovary, for histologic diagnosis.	Blood-clot undergoing necrotic change.	2294—Inoculation from lung, to determine character of infection.	Sterile.
2271—Tissue from thigh, for histologic diagnosis.	Adipose tissue	2295—Inoculation from fluid from lung, to determine character of infection.	Sterile.
2272—Blood, for Widal's test.	Negative.*	2296—Blood, for Widal's test.	Negative.*
2273—Blood, for Widal's test.	Negative.*	2297—Growth from eyelid, for histologic diagnosis.	Tubular epithelioma.
2274—Blood, for Widal's test.	Positive.	2298—Cervical glands, for histologic diagnosis.	Chronic caseous tuberculous lymphadenitis.
		2299—Blood, for Widal's test.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2300—Blood, for Widal's test.	Negative.*	2326—Inoculation from throat, to determine character of in- fection.	Bacillus diphtheriae and Streptococcus lanceolatus.
2301—Wart from nose, for histo- logic diagnosis.	Cystic papilloma.	2327—Material from ilio-psoas bursa, for histologic diag- nosis.	Hydrops of ilio-psoas bursa.
2302—Gastric contents.	Negative.*	2328—Tissue from neck, for histo- logic diagnosis.	Chronic tuberculous adenitis.
2303—Blood count.	Anemia.	2329—Inoculation from ilio-psoas bursa, to determine char- acter of infection.	Sterile.
2304—Urine.	Negative.*	2330—Omentum, for histologic diagnosis.	Fat necrosis.
2305—Inoculation from brain, to determine character of in- fection.	Sterile.	2331—Mass from eye, for histo- logic diagnosis.	Squamous-cell epithelioma.
2306—Tissue from brain, for histo- logic diagnosis.	Round-cell sarcoma.	2332—Blood, for bacteriological examination.	Negative.*
2307—Inoculation from boil, to determine character of in- fection.	Staphylococcus pyogenes albus.	2333—Blood, for Widal's test.	Positive.
2308—Blood, for Widal's test.	Negative.*	2334—Portion of pleura, for histo- logic diagnosis.	Chronic productive pleuritis and chronic interstitial myositis.
2309—Wart from nose, for histo- logical diagnosis.	Papilloma.	2335—Inoculation from empye- ma, to determine character of infection.	Streptococcus pyogenes.
2310—Mamma and axillary glands, for histologic diag- nosis.	Scirrhus carcinoma.	2336—Slide, for histologic diag- nosis.	Spindle-cell sarcoma.
2311—Tissue from (a) forehead, (b) cheek, for histologic diagnosis.	Papillomata.	2337—Portion of muscle, for histo- logic diagnosis.	Myositis.
2312—Blood, for Widal's test.	Negative.*	2338—Blood, for Widal's test.	Negative.*
2313—Fluid from pleura, for bac- teriologic examination.	Negative.*	2339—Blood, for Widal's test.	Negative.*
2314—Sputum, for tubercle bacilli.	Present.	2340—Superior maxilla, for histo- logic diagnosis.	Squamous-cell epithelioma.
2315—Tissue from popliteal nerve, for histologic diag- nosis.	Fibromyoxoma.	2341—Mamma, for histologic di- agnosis.	Fibro-adenoma.
2316—Portion of tongue, for histo- logic diagnosis.	Chronic ulcer.	2342—Inoculation from thigh, to determine character of in- fection.	Negative.*
2317—Gland from groin, for histo- logic diagnosis.	Suppurating lymphatic gland.	2343—Mamma, for histologic di- agnosis.	Cystic involution.
2318—Blood, for Widal's test.	Negative.*	2344—(a) Breast, (b) supra-cla- vicular gland, for histologic diagnosis.	(a) Scirrhus carci- noma. (b) Hyperplasia.
2319—Inoculations from vaginal discharge.	Streptococcus pyo- genes, and Staphylococcus pyogenes albus.	2345—Blood, for Widal's test.	Negative.*
2320—Placenta and membranes, for histologic diagnosis.	Negative.*	2346—Tumor from jaw, for histo- logic diagnosis.	Myxosarcoma.
2321—Rectal polyp, for histologic diagnosis.	Received in a condi- tion not suitable for examination.	2347—Inoculation from lung, to determine character of in- fection.	Staphylococcus pyogenes albus.
2322—Material from stools, for histologic diagnosis.	Inflammatory tissue.	2348—Section of lung (?) tissue, for histologic diagnosis.	Muscle; Chronic interstitial myositis; ossifying fibrous tissue
2323—Supraclavicular glands, for histologic diagnosis.	Metastatic scirrhus carcinoma.	2349—Ulcer of tongue, for histo- logic diagnosis.	Squamous-cell epithelioma.
2324—Mamma, for histologic di- agnosis.	Scirrhus carcinoma.	2350—Stone, for examination.	Biliary calculus, pigment and chole- sterin.
2325—Hard and soft palate, for histologic diagnosis.	Endothelioma.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2351—Inoculation from wrist-joint, to determine character of infection.	<i>Bacillus typhosus</i> , and <i>Staphylococcus pyogenes aureus</i> .	2376—Inoculation from chest wall, to determine character of infection.	Sterile.
2352—Bone from wrist, for histologic diagnosis.	Normal bone.	2377—Discharge, for bacteriologic examination.	<i>Pneumococcus</i> , and <i>Bacillus</i> of Friedländer.
2353—Tapeworm, for diagnosis	<i>Tænia mediocanellata</i> .	2378—Fluid from pleura, for bacteriologic examination.	Negative.*
2354—Inoculation from hand, to determine character of infection.	<i>Staphylococcus pyogenes aureus</i>	2379—Blood, for Widal's test.	Negative.*
2355—Inoculation from hand, to be examined for <i>Bacillus tetani</i> .	Negative.*	2380—Blood, for Widal's test.	Negative.*
2356—Inoculation from neck, to be examined for <i>Bacillus tetani</i> .	Negative.*	2381—Blood, for Widal's test.	Negative.*
2357—Inoculation from hand, to be examined for <i>Bacillus tetani</i> .	Negative.*	2382—Blood, for Widal's test.	Negative.*
2358—M a m a, for histologic diagnosis.	Scirrhus carcinoma.	2383—Tissue from tongue, for histologic diagnosis.	Squamous-cell epithelioma.
2359—Tissues from autopsy, for histologic diagnosis.	Ulcerative cervicitis uteri.	2384—Blood, for Widal's test.	Negative.*
2360—Glands from neck, for histologic diagnosis.	Tubercular lymphadenitis.	2385—Mass from rectum, for histologic diagnosis.	Cylindric-cell carcinoma.
2361—M a m a, for histologic diagnosis.	Glandular carcinoma.	2386—(1) Mass from foot, (2) glands from groin, for histologic diagnosis.	Alveolar mixed-cell, melanotic sarcoma of foot with metastases to lymph glands.
2362—Inoculation from neck, to determine character of infection.	<i>Bacillus megatherium</i> , and <i>Staphylococcus pyogenes albus</i> .	2387—Inoculation from nerve, to determine character of infection.	<i>Staphylococcus pyogenes aureus</i> .
2363—Cerebro-spinal fluid, for bacteriologic examination.	Negative.*	2388—Blood, for Widal's test.	Negative.*
2364—Blood, for Widal's test.	Negative.*	2389—Urine, to be examined for lead.	Negative.*
2365—Tumor from ovary, for histologic diagnosis.	Cystic ovaritis.	2390—Blood, for Widal's test.	Negative.*
2366—Tissue from tongue, for histologic diagnosis.	Tuberculous ulcer.	2391—Inoculation from chin, to determine character of infection.	Sterile.
2367—Recurrent tumor from arm, for histologic diagnosis.	Large, spindle-cell, melanotic sarcoma.	2392—Mass from axilla, for histologic diagnosis.	Squamous-cell epithelioma.
2368—Tissue from cheek and superior maxilla, for histologic diagnosis.	Squamous epithelioma.	2393—Tissue from (a) neck, (b), jaw, for histologic diagnosis	(a) Chondrosarcoma undergoing cystic and myxomatous degeneration. (b) Alveolar sarcoma.
2369—Blood, for Widal's test.	Positive.	2394—M a m a, for histologic diagnosis.	Chronic interstitial mastitis; cystic degeneration.
2370—Tumor from side of head, for histologic diagnosis.	Cutaneous papilloma; multiple sebaceous cysts with intracystic papillomata.	2395—Testicle and tissue from scrotum, for histologic diagnosis.	Infected squamous-cell epithelioma.
2371—Mass from iliac cavity, for histologic diagnosis.	Blood clot.	2396—Section of nerve, for histologic diagnosis.	Chronic neuritis.
2372—M a m a, for histologic diagnosis.	Scirrhus carcinoma.	2397—Tissue from lip, for histologic diagnosis.	Squamous-cell epithelioma.
2373—Tissue from mamma, for histologic diagnosis.	Peri- and intracanalicular fibroma.	2398—Blood, for Widal's test.	Negative.*
2374—Blood, for Widal's test.	Negative.*	2399—Blood, for Widal's test.	Negative.*
2375—Nerves, for histologic diagnosis.	Chronic interstitial and parenchymatous neuritis; fibrous tissue.	2400—Urine.	Negative.*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2401—Urine.	Nephritis.	2426—Feces, for bacteriologic examination.	See No 2422.
2402—Blood, for Widal's test.	Positive.	2427—Urine.	Negative.*
2403—Blood, for Widal's test.	Negative.*	2428—Blood, for Widal's test.	Negative.*
2404—Blood, for Widal's test.	Negative.*	2429—Blood, for Widal's test.	Negative.*
2405—Tissue from breast, for histologic diagnosis.	Fibro-adenoma.	2430—Epididymus, for histologic diagnosis.	Tubercular epididymitis.
2406—Blood, for Widal's test.	Negative.*	2431—Fluid from ovary, for bacteriologic examination.	Negative.*
2407—Blood, for Widal's test.	Negative.*	2432—Blood, for malaria organisms.	Negative.*
2408—Feces, for dysentery bacilli	Negative.*	2433—Urine.	Pyuria.
2409—Ulcer of skin, for histologic diagnosis.	Infected ulcer.	2434—Spreads from meningeal exudate, for bacteriologic examination.	Bacillus tuberculosis.
2410—Inoculation from abscess, to determine character of infection.	Sterile.	2435—Organs from autopsy, for histologic diagnosis.	Tuberculous meningitis.
2411—Blood, for Widal's test.	Negative.*	2436—Mamma, and node from sternum, for histologic diagnosis.	Scirrhus carcinoma.
2412—Tissue from uterus, for histologic diagnosis.	Papillary adenocystoma.	2437—Blood.	Anemia.
2413—Gland of neck, for histologic diagnosis.	Perithelioma of parotid.	2438—Sputum, for tubercle bacilli.	Present.
2414—Blood, for Widal's test.	Negative.*	2439—Urine.	Albuminuria.
2415—(a) Portion of tongue, (b) submaxillary gland, (c) lymph gland, for histologic diagnosis.	(a) Squamous epithelioma. (b) Acute non-suppurative interstitial inflammation. (c) Acute simple lymphadenitis.	2440—Pleural effusion, for bacteriologic examination.	Negative.*
2416—Epididymus, for histologic diagnosis.	Tubercular epididymitis.	2441—Inoculation from gall-bladder, to determine character of infection.	Bacillus pseudodysentericus.
2417—Glans penis, for histologic diagnosis.	Chronic healed-in ulcer.	2442—Pus from pleura, for bacteriologic examination.	Bacillus pyocyaneus.
2418—Appendix, for histologic diagnosis.	Chronic interstitial, chronic ulcerative, and acute catarrhal appendicitis.	2443—Inoculation from neck, to determine character of infection.	Sterile.
2419—Inoculations from abscess of foot, to determine character of infection.	Staphylococcus pyogenes aureus, Proteus vulgaris, and Bacillus pyogenes fetidus.	2444—Maxilla, for histologic diagnosis.	Small round-cell sarcoma.
2420—Blood, for Widal's test.	Positive.	2445—Tumor from antrum of Highmore, for histologic diagnosis.	Small round-cell, melanotic sarcoma.
2421—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	2446—Mamma, for histologic diagnosis.	Interstitial mastitis with cystic degeneration.
2422—Feces, for bacteriologic examination.	Intestinal tuberculosis(?)	2447—Blood clot from temporal region, for bacteriologic examination.	Sterile.
2423—Blood, for Widal's test.	Negative.*	2448—Urine.	Albuminuria.
2424—Blood, for Widal's test.	Negative.*	2449—Blood, for Widal's test.	Negative.*
2425—Tissue from neck, for histologic diagnosis.	Branchial cyst.	2450—Urine.	Negative.*
		2451—Inoculation from empyema to determine character of infection.	Staphylococci pyogenes aureus and albus.
		2452—Glands from neck, for histologic diagnosis.	Chronic hyperplastic lymphadenitis.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2453—Blood, for Widal's test.	Negative.*	2481—Blood, for Widal's test.	Positive.
2454—Blood, for Widal's test.	Negative.*	2482—Inoculation from leg, to determine character of in- fection.	Sterile.
2455—Inoculations from gall blad- der, to determine character of infection.	Sterile. Bile pigment and cholesterin calculus.	2483—Inoculation from femur, to determine character of in- fection.	Staphylococcus pyogenes aureus.
2456—Inoculations from gall blad- der, to determine character of infection.	Staphylococcus pyogenes albus.	2484—Inoculation from vaginal discharge, to determine character of infection.	Bacillus coli com- munis. Staphylococ- cus pyogenes aureus.
2457—Blood, for Widal's test.	Negative.*	2485—Blood, for Widal's test.	Positive.
2458—Sac from spina bifida, for histologic diagnosis.	Chronic productive inflammation.	2486—Blood, for Widal's test.	Negative.*
2459—Blood, for Widal's test.	Negative.*	2487—Blood, for Widal's test.	Negative.*
2460—Blood count.	Polycythemia.	2488—Tumor from jaw, for histo- logic diagnosis.	Secondary carci- noma.
2461—Blood, for Widal's test.	Positive.	2489—Pleura and ribs, for histo- logic diagnosis.	Empyema.
2462—Pleural effusion, for bacter- iologic examination.	Pneumococcus.	2490—Tissue from liver, for histo- logic diagnosis.	Cirrhosis, atrophic.
2463—Tissue from lip, for histo- logic diagnosis.	Cavernous angioma.	2491—Tissue from nose, for histo- logic diagnosis.	Inflammatory new formation. Chronic interstitial myositis.
2464—Gland from neck, for histo- logic diagnosis.	Salivary gland, showing slight inter- stitial inflammation	2492—Blood, for Widal's test.	Negative.*
2465—Blood, for Widal's test.	Positive.	2493—Hand, tissue from, for histo- logic diagnosis.	Received in condi- tion not suitable for examination.
2466—Scrapings from uterus, for histologic diagnosis.	Glandular endometritis.	2494—Inoculation from autopsy, to determine character of infection.	Staphylococcus pyogenes aureus.
2467—Blood, for Widal's test.	Negative.*	2495—Organs obtained postmor- tem, for histologic diag- nosis.	Septic pneumonia
2468—Pus from pleura, for bacter- iologic examination.	Staphylococcus pyogenes aureus.	2496—Blood, for Widal's test.	Positive.
2469—Blood, for Widal's test.	Negative.*	2497—Breast, for histologic diag- nosis.	Chronic productive interstitial mastitis; cystic involution.
2470—Blood, for Widal's test.	Negative.*	2498—Blood, for bacteriologic ex- amination.	Staphylococcus pyogenes aureus.
2471—Pus from dorsum of penis, for bacteriologic examina- tion.	Bacillus coli communis.	2499—Inoculation from humerus, to determine character of infection.	Staphylococcus pyogenes aureus.
2472—M a m m a and axillary glands, for histologic di- agnosis.	Scirrhus carcinoma.	2500—Tract of sinus, for histo- logic diagnosis.	Granulating sinus.
2473—Sputum, for tubercle bac- illi.	Present.	2501—Inoculation from breast, to determine character of in- fection.	Sterile.
2474—Glands from neck, for histo- logic diagnosis	Chronic, caseous, tuberculous lymph- adenitis.	2502—Blood, for bacteriologic examination.	Staphylococcus pyogenes albus.
2475—Tissue from nose, for histo- logic diagnosis.	Soft fibroma.	2503—Tissue from floor of mouth, for histologic diagnosis.	Leukoplakia.
2476—Tissue from sacral region, for histologic diagnosis.	Sacral teratoma.	2504—Tube and ovary, for histo- logic diagnosis.	Hematic cyst; ovar- ian apoplexy; chro- nic sclerosing oöphoritis.
2477—Blood, for Widal's test.	Negative.*	2505—Blood, for bacteriologic examination.	Negative.*
2478—Blood, for Widal's test.	Negative.*		
2479—Gland from back, for histo- logic diagnosis.	Squamous-cell epithelioma.		
2480—Glands from neck, for histo- logic diagnosis.	Chronic, caseous, tuberculous lymphadenitis.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2506—Blood, for Widal's test.	Positive.	2531—Tissue from cheek, for histologic diagnosis.	Squamous-cell epithelioma.
2507—Blood, for Widal's test.	Positive.	2532—Blood, for Widal's test.	Negative.*
2508—Tissue from jaw, for histologic diagnosis.	Lymphangio-endothelioma.	2533—Inoculation from cheek, to determine character of infection.	Pneumococcus, and Micrococcus pyogenes fretidus.
2509—Goitre, for histologic diagnosis.	Cystic goitre.	2534—Blood, for bacteriologic examination.	Negative.*
2510—Tissue from nose, for histologic diagnosis.	Papilloma.	2535—Inoculation from abdominal cavity, to determine character of infection.	Sterile.
2511—Blood, for Widal's test.	Positive.	2536—Blood, for Widal's test.	Positive.
2512—Stools, for Bacillus dysenteriae.	Negative.*	2537—Tumor from back, for histologic diagnosis.	Melanotic round-cell sarcoma.
2513—Inoculation from gums, to determine character of infection.	Streptococcus pyogenes.	2538—Organs from autopsy, for histologic diagnosis.	Sarcomatosis.
2514—Inoculations from nodules in axilla, to determine character of infection.	Sterile.	2539—Urine.	Negative *
2515—Nodule from anterior chest wall, for histologic diagnosis.	Hodgkin's disease.	2540—Bone from skull, for histologic diagnosis.	Slight absorption of bone.
2516—Mass from axilla, for histologic diagnosis.	Hodgkin's disease.	2541—Fluid from pleura, for bacteriologic examination.	Negative.*
2517—Sputum for tubercle bacilli.	Negative.*	2542—Water, for bacteriologic examination.	Negative.*
2518—Inoculation from mouth, to determine character of infection.	Streptococcus pyogenes	2543—Tumor from neck, for histologic diagnosis.	Endothelioma.
2519—Blood, for bacteriologic examination.	Sterile.	2544—Tumor from face and parotid gland, for histologic diagnosis.	Perithelioma.
2520—Cyst from neck, for histologic diagnosis.	Branchial cyst.	2545—Inoculation from back, to determine character of infection.	Bacillus pyocyaneus, and Staphylococcus pyogenes aureus.
2521—Tissue from jaw, for histologic diagnosis.	Infected squamous-cell epithelioma.	2546—Kidney, for histologic diagnosis.	Hypernephroma; slight chronic diffuse nephritis.
2522—Section of ulnar nerve, for histologic diagnosis.	Chronic parenchymatous and interstitial neuritis.	2547—Tumor from breast, for histologic diagnosis.	Galactoceles. Acute non-suppurative interstitial mastitis; slight productive mastitis.
2523—Inoculation from femur, to determine character of infection.	Sterile.	2548—Inoculation from kidney, to determine character of infection.	Sterile.
2524—Inoculation from neck, to determine character of infection.	Sterile.	2549—Ulcer from face, for histologic diagnosis.	Squamous-cell epithelioma.
2525—Mass from eye, for histologic diagnosis.	Tuberculosis.	2550—Milk, for bacteriologic examination.	Tubercle bacilli.
2526—Inoculation from eye, to determine character of infection.	Staphylococcus pyogenes albus.	2551—Tumor from brain, for histologic diagnosis.	Fibrosarcoma.
2527—Tumor from rectum, for histologic diagnosis.	Fibromyoma.	2552—Inoculation from brain tumor, to determine character of infection.	Sterile.
2528—Tissues from autopsy, for histologic diagnosis.	Hodgkin's disease.	2553—(a) Urine, (b) Sputum.	(a) Albuminuria. (b) Negative.*
2529—Inoculation from cheek, to determine character of infection.	Staphylococcus pyogenes aureus.	2554—Blood count.	Negative.*
2530—Feces, for bacteriologic examination, ameba, etc.	Ameba.	2555—Inoculation from neck, to determine character of infection.	Staphylococcus pyogenes aureus.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2556—Urine.	See No. 2553 (a).	2559—Inoculation from fluid from chest, to determine char- acter of infection.	Sterile.
2557—Urine.	Negative.*		
2558—Piece of omentum, for his- tologic diagnosis.	Received in condi- tion not suitable for examination.	2560—Goitre, for histologic diag- nosis.	Parenchymatous goitre.

* The word "negative" is used in this report to mean, (1) The material or body which the examination was conducted to demonstrate was not present. (2) No information of diagnostic importance was obtained. Thus a blood or urinary examination yielding no diagnostic aid is marked "negative." The same word is used when, for example, the Widal test was applied without the occurrence of clumping. The different applications will be apparent.

PUBLICATIONS
FROM THE
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OF THE
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INTRODUCTION.

The articles comprising this volume are reprints of papers published in various periodicals. They are assembled as permanent records of part of the work done and also for the convenience of those interested in Laboratory investigations. Some represent studies of material obtained from operations and autopsies, while others are based on original inquiry made in the Laboratories of the Jefferson Medical College Hospital. The work also contains a tabulated summary of the examinations conducted in the Laboratories during the year ending December 31, 1904.

W. M. L. COPLIN,
Director.

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Albert B. Craig was born in Missouri in 1867. After a varied experience he entered Jefferson Medical College in 1898, and graduated with honors in the class 1901, his previous work leading to the degree of A. B. enabling him to complete the course in three years. He served as Interne in the Jefferson Hospital and was then honored by Professor Keen, who chose him as a Junior Assistant in his private work. Later he was appointed Demonstrator of Surgery and Assistant Demonstrator of Anatomy in the Jefferson College, and his literary ability secured for him a position on the editorial staff of American Medicine. The circumstances surrounding Dr. Craig's death, March 14, 1905, were peculiarly sad and served to bring out in strong relief the true character of the man. Called professionally to the bedside of a young acquaintance suffering from cerebrospinal meningitis, he proved truly a physician and a friend, giving freely of his time both day and night to minister to his charge. Shortly after the death of his friend, Dr. Craig felt the symptoms of the dread disease and in less than twenty-four hours died in agony. The history of those few hours, during the first of which only the doomed man himself knew his condition, as he put in order his affairs and took leave of his bride of but a few months, recalls the heroism of other martyrs. His whole life had been a brave struggle in the face of difficulties and to it his heroic behavior at the last was a fitting climax. Verily he gave his life to his profession and, though unavailing, for his friend. Of him, what more need mortal say !



A.B. Craig

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**AN EXPERIMENTAL AND HISTOLOGICAL STUDY
OF CARGILE MEMBRANE.¹**

WITH REFERENCE TO (1) ITS EFFICACY IN PREVENTING ADHESIONS IN THE
ABDOMINAL AND CRANIAL CAVITIES AND AROUND NERVES AND TENDONS,
AND (2) ITS ULTIMATE FATE IN THE TISSUES.

BY ALBERT B. CRAIG, M.D.,²

OF PHILADELPHIA,

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AND

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(From the Laboratories of the Jefferson Medical College Hospital.)

EXPERIMENTAL STUDY BY DR. CRAIG.

It is not worth while to attempt an enumeration of the efforts which have been made to prevent adhesions in the peritoneal cavity; nor is it necessary to lay stress upon the necessity for preventing such adhesions when it can be accom-

¹Read before the Philadelphia Academy of Surgery, February 6, 1905.

²The death of Dr. Craig, March 14, 1905, from cerebrospinal meningitis, contracted while in attendance upon a patient suffering from that disease, lends additional interest to this report of his latest study.

plished. Adhesions within this cavity are, on the whole, beneficial, however harmful under certain circumstances. We cannot expect Nature to differentiate; it is left to the devices of the surgeon to prevent, if he can, adhesions when they would be harmful, and, in truth, it may be stated that he has succeeded but poorly.

In May, 1902 (*Medical Record*, May 17, 1902), Dr. Robert T. Morris, of New York, published the results of a series of experiments carried out upon rabbits, to determine the value of a specially prepared animal membrane derived from the peritoneum of the ox. The effort was made to prevent adhesions within the peritoneal cavity. Attention was first called to this membrane by Dr. Charles Cargile, of Bentonville, Arkansas, who sent Dr. Morris specimens of the membrane to be used, hence the New York surgeon termed the material Cargile membrane, an eponym which has since become common. The membrane is not essentially different from gold-beaters' skin, except in the method of its preparation. As prepared by Johnson and Johnson, it comes in small sheets about eight by sixteen centimetres in size, and is treated after a special method. Some of it is treated evidently somewhat after the manner of chromicized catgut, and is hence termed chromicized Cargile membrane; another preparation is unchromicized. The report of Dr. Morris, on the whole, was favorable, and he appeared to believe that the membrane possessed distinct advantages in preventing adhesions. His conclusions, somewhat abridged, were as follows: Cargile membrane seems to resist absorption in the peritoneal cavity for more than ten days and less than thirty days. Its presence apparently causes the formation of temporary loose adhesions, which are harmless, and which become absorbed for the most part in less than thirty days. The membrane seems to cause very little disturbance to the peritoneum; it does not furnish a good culture medium for bacteria, and it protects areas of peritoneal surface that have suffered injury to their endothelial covering, until new endothelial cells have repaired the injury without involving the neighboring peritoneum. It is not

necessary to suture the membrane in place, as it becomes instantly adherent to moist surfaces, and is not readily dislodged afterwards.

If the membrane possessed the merits which Dr. Morris's experiments seemed to warrant, I could not understand why surgeons did not make more general use of it as a protective covering for surfaces denuded of peritoneum, and in other situations in which it would appear applicable.

To satisfy myself of the value, or the reverse, of this membrane, in the summer of 1904 I undertook a series of experiments in the laboratories of the Jefferson Medical College Hospital. The membrane was kindly furnished me by the manufacturers above mentioned. Dogs were used in the experiments, and not only were tests made in the peritoneal cavity, but likewise in the protection of tendons and nerves, and the cranial cavity was invaded. After various intervals of time the seat of operation was exposed in each case, the clinical conditions ascertained, and, in a number of instances, specimens of tissue which had been in contact with the membrane were submitted to Dr. Ellis, associate in pathology at the College, who kindly undertook the microscopic investigations in this research. His findings are set forth in a separate portion of this paper.

It will be noted in the following recitation of the experiments, that when Cargile membrane was used in the peritoneal cavity of a dog, in most instances the membrane was anchored in place by fine silk sutures. It was of course recognized that the irritation produced by the sutures would, in a measure, vitiate the experiment; but it was believed, and subsequent experiments showed the assumption warranted, that if a sufficiently large piece of membrane were used, so that the suture could be placed on either side of the intestine well towards the mesenteric attachment, the irritation produced by them need not interfere with the surface opposite that attachment. Furthermore, it was found by simple tests that the statement of Dr. Morris, namely, that the membrane would adhere readily and sufficiently to a denuded surface without

suturing, was correct so long as the peritoneal, or denuded surface, was dry, or relatively so; but directly the intestine with the attached membrane was returned to the peritoneal cavity and bathed for a short time in the peritoneal fluid, the membrane ceased to adhere and readily slipped from the particular point covered. With this fact, repeatedly demonstrated, in mind, we of course could not expect that the membrane would adhere and remain where placed, despite the various movements of the animal and the peristaltic activity of the abdominal viscera. I therefore anchored the membrane by sutures, to be sure that it remained *in situ* over the denuded area. It is conceivable that Cargile membrane may be placed in the pelvis or similar situations, between the peritoneum and a denuded surface, or between denuded surfaces, and remain in place without being anchored. It certainly will not remain, when unanchored, on either visceral or parietal surfaces when these are bathed in fluids and subjected to friction, be it never so little, from peristaltic activity. I may state in passing that I tried anchoring by means of celloidin and also by means of formalin-gelatin. Neither was a success.

All the dogs operated upon were profoundly anesthetized with ether and treated according to the rules of aseptic surgery, so far as could be conveniently carried out. In only one instance did peritonitis occur, and this was from a defective end-to-end anastomosis.

EXPERIMENT No. I.—The abdominal cavity of a dog having been opened, a loop of intestine near the stomach was lifted out and two surfaces opposite the mesenteric attachment, each one and one-half centimetres square, were denuded of peritoneum, sponged until dry, covered with separate pieces of unchromicized Cargile membrane without anchoring, the abdominal wound being closed with silk-worm-gut sutures. Twelve days later the abdomen was reopened and a mass of omentum was fairly firmly adherent to the distal denuded surface, and both omentum and liver were adherent to the proximal denuded surface; no Cargile membrane was found; either it did not remain *in situ*, or it had been absorbed and adhesions formed subsequently.

EXPERIMENT No. II.—The abdomen of a dog was opened and a loop of small intestine was brought out. A surface one centimetre by one and one-half centimetres was denuded of peritoneum and covered with

chromicized membrane, the piece being large enough to extend back on either side to the mesenteric attachment, where it was anchored by sutures. Ten centimetres distal to this was anchored in like manner a piece of unchromicized membrane over an undenuded surface; further distal by ten centimetres was anchored similarly, a piece of chromicized membrane over a denuded surface; while still distal to this was anchored a sheet of chromicized membrane over an undenuded surface. In this experiment I sought to compare the effects of placing chromicized and unchromicized membrane each on denuded and undenuded surfaces. The sutures were so placed that I could identify the several pieces. Fourteen days later, forty centimetres of the bowel containing the four separate experiments were resected, examined macroscopically, and submitted to Dr. Ellis for microscopic examination. It was of interest to note that while a mass of adherent omentum completely covered the site of operation in each case, and a loop of bowel was adherent in two places, yet the Cargile membrane was at no place completely absorbed; both the chromicized and unchromicized membranes were clearly detected by splitting the mass of adherent omentum. The latter was adherent directly to the membrane, and more firmly still to the bowel at the periphery of the membrane. Under the membrane the denuded area was rough and scar-like, and there was no macroscopic evidence of regenerating peritoneum. Clearly, used in this manner, the membrane would not prevent adhesions.

EXPERIMENT No. III.—The abdomen of a dog was opened and two areas of the duodenum seven centimetres apart and each one and one-half by two centimetres in area were denuded of peritoneum, and the proximal one was covered with unchromicized Cargile membrane, while the distal one was left with its raw surface exposed. At the same operation an area two centimetres square on the anterior surface of the stomach was denuded of peritoneum and covered similarly with unchromicized membrane, but the latter was not anchored by suture. The abdominal wound was closed in the usual way. Nineteen days later the abdomen was reopened and firm adhesions were found at each site of denudation. Apparently they were as firm and as numerous where the Cargile membrane had been placed as where it had not been placed. A careful search revealed no Cargile membrane.

EXPERIMENT No. IV.—The abdomen of a dog was opened and four pieces of Cargile membrane were placed as follows: (a) A piece of unchromicized membrane was placed over a denuded surface one by two centimetres in size and anchored well towards the mesenteric attachment; (b) a piece of unchromicized membrane was placed over an undenuded surface and similarly anchored; (c) a piece of chromicized membrane was placed over a denuded surface of similar size and anchored, as above; and (d) a piece of chromicized membrane was placed over an undenuded surface and attached by sutures as in the foregoing. The number of sutures differed with each piece anchored, so that the several pieces could be recognized. Four days later the abdomen was again opened and thirty-

five centimetres (fourteen inches) of the bowel, to which the four pieces of membrane had been attached, was resected and end-to-end anastomosis done. Adherent omentum completely covered and surrounded every piece of membrane. The adhesions were easily broken up, being so recent, but they were numerous. At the two places where the unchromicized membrane was placed, none of the Cargile membrane could be found macroscopically, though Dr. Ellis was able to find fragments microscopically. The chromicized membrane, however, was plainly visible where it had been placed. Neither had prevented adhesions, particularly at the periphery of the membrane. The resected portion of the intestine was submitted to Dr. Ellis for microscopic examination.

EXPERIMENT No. V.—A dog's abdomen was opened and an area one and one-half by four centimetres was denuded of peritoneum and covered with unchromicized membrane. It was anchored *in situ* as above explained. Ten centimetres distal to this, an area one and one-half by two centimetres was similarly denuded, but left exposed without Cargile covering. The abdomen was closed and sixteen days later reopened. A mass of omentum covered the entire site of operation in each instance, and no membrane was found.

EXPERIMENT No. VI.—A dog's abdomen was opened and a surface one and one-half by three centimetres on the duodenum was denuded of peritoneum and covered with the unchromicized membrane, the edges being anchored as in previous instances. Ten centimetres distal to this a similar area was denuded and not covered with membrane. Eleven days later the abdomen was reopened and fairly firm adhesive omentum covered alike both areas. No membrane was found.

EXPERIMENT No. VII.—A dog's abdomen having been opened, an area one and one-half by two centimetres on the duodenum was denuded of peritoneum and covered with unchromicized Cargile membrane, the latter being anchored as above. Three days later the abdomen was reopened. A large omental graft had covered the entire site of operation. The membrane immediately covering the actual denudation had disappeared, but it persisted in the rest of its extent; that is, the centre of the sheet of membrane had been digested or dissolved by the raw surface. This showed that some element in the actual wound acted, probably in a digestive capacity, in dissolving the membrane in immediate contact. A portion of the intestine containing the field of operation was resected and submitted for microscopic examination.

EXPERIMENT No. VIII.—A dog's abdomen having been opened, a small area of duodenum was denuded of peritoneum, covered with unchromicized membrane which was anchored by sutures, and this in turn was covered by a piece of sterile rubber dam which extended well beyond the Cargile membrane; this, too, was in turn anchored by suture. Three days later the abdomen was reopened, and it was found that a mass of omentum and aplastic lymph completely covered the entire site of operation, including the rubber dam. I desired by this experiment to determine whether it was a phagedenic property of the omentum that

destroyed the membrane, or was it granulation tissue, or was it peritoneal fluid? The mass was removed from the rubber dam; the latter was likewise carefully removed and no Cargile membrane was recognized macroscopically, though fragments were observed by Dr. Ellis microscopically.

EXPERIMENT No. IX.—This was a repetition of Experiment VIII, except that the abdomen was reopened on the sixth day instead of the third after operation. Practically, the same conditions were found, namely, the sheet of rubber dam, under which the Cargile membrane had been placed, was covered with an omental graft, and on examination the Cargile membrane had all disappeared to macroscopic view, though seen by Dr. Ellis microscopically.

EXPERIMENT No. X.—Experiments VIII and IX appeared to offer fair evidence that it was not the omentum *per se* that had destroyed the membrane, but it proved nothing as to the action of the peritoneal fluid. Accordingly, I placed a piece of unchromicized membrane, five centimetres square and made into a small roll, in a glass tube one centimetre in diameter and seven and one-half centimetres long, and containing about a dozen small perforations; in another tube of about equal size was placed a similar piece of the chromicized variety. These tubes were closed sufficiently to prevent the escape of the membrane and placed loose in the peritoneal cavity of a dog. Fourteen days later the abdomen was reopened and both tubes were easily found. The tube containing the chromicized membrane was practically free, and when removed the membrane was quite softened, pale, and œdematous, but apparently little changed in other respects. It was delivered to Dr. Ellis for further examination. The tube which had contained the unchromicized membrane was wrapped about with omentum, but the membrane had entirely disappeared, leaving the tube empty. Clearly, the chromicized membrane was much the more resistant.

EXPERIMENT No. XI.—From the glass-tube experiments we had fair proof that the unchromicized membrane would soon disappear when placed in the abdominal cavity, without actual contact with the omentum. It appeared a natural deduction that the peritoneal fluid could itself be potent in dissolving the membrane. To exclude the phagocytic action of the leucocytes, at Professor Coplin's suggestion and under his direction, I placed a piece of unchromicized membrane three centimetres square in a celloidin capsule five centimetres long, containing salt solution. Pathologists state that this capsule will permit the osmosis of the body fluids, but leucocytes will not pass through its wall. The sealed capsule, with the contained membrane, was placed free in the abdominal cavity of a dog. On the seventh day the capsule was removed and opened. The membrane, aside from being œdematous and apparently thickened, was little changed macroscopically. There was little fluid left in the capsule. The membrane was submitted to Dr. Ellis.

EXPERIMENT No. XII.—The above experiment was repeated in every detail, except the celloidin capsule was not removed until the thirtieth day. It was easily found wrapped in a small mass of omentum. There was apparently no infection. Professor Coplin opened the capsule. It

contained a milky, slightly blood-stained fluid, and the membrane, hardly recognizable as such, just at the point of disintegration. It had apparently almost dissolved. Professor Coplin examined some of the fresh fluid from the capsule under the microscope. The findings are detailed in the paper of Dr. Ellis.

EXPERIMENT No. XIII.—The left tendo-Achillis and the left posterior tibial nerve of a dog were exposed, and each was wrapped separately with four turns of unchromicized Cargile membrane. At the same operation the right tendo-Achillis and accompanying posterior tibial nerve were exposed and wrapped with three turns of chromicized Cargile membrane. The wounds were sutured. Fourteen days later the dog was killed and three centimetres of each tendon and its accompanying nerve were resected *en masse*. Examined macroscopically, the right nerve, around which the chromicized membrane had been placed, showed the membrane still in place; and while there was a mass of granulation tissue outside the membrane, the latter had plainly protected the nerves, there being no macroscopic adhesions to the latter whatever, except at either end of the tube formed by the protecting Cargile membrane. The left nerve, about which the unchromicized membrane had been placed, showed no Cargile membrane macroscopically, though microscopic fragments were found by Dr. Ellis. And while adhesions to the nerve were distinctly fewer and less firm where it had been protected by the membrane than where it had not, yet fairly firm adhesions (for fourteen days) were present, and it was evident that the nerve had not been so well protected as where the chromicized membrane had been employed.

EXPERIMENT No. XIV.—Under ether the two tendons, as above mentioned, of a dog were exposed for a distance of five centimetres, and when each tendon was raised from its bed it was wrapped about by two turns of unchromicized membrane and the skin wound was closed. Twenty days later the dog was killed, and both tendons and the accompanying posterior tibial nerves were removed. Plainly, there were fairly firm adhesions to the tendon, more marked than at points not subjected to trauma. No membrane was found. The specimens were submitted to Dr. Ellis.

EXPERIMENT No. XV.—The right tendo-Achillis of a dog was exposed, lifted from its bed, and four turns of unchromicized Cargile membrane were passed around it, thus isolating it completely. The accompanying posterior tibial nerve was isolated, wrapped separately with two turns of membrane, and plaster dressing was applied to the dog's leg. It was hoped by immobilizing the parts that a better idea of the actual protection afforded by the membrane, if any, could be had. Inability to keep the wound aseptic necessitated the removal of the plaster dressing. Five days after operation the wound was reopened. A mass of granulation tissue surrounded the tendon and nerve, but not a vestige of Cargile membrane could be found. Plainly, it had afforded little or no protection. It could only be assumed that the granulation tissue would follow the usual course and result in scar tissue, thus causing adhesion, unless constant motion prevented.

EXPERIMENT No. XVI was a repetition of Experiment XV, except that, in addition to covering the nerve and tendon separately, a piece of Cargile membrane two and one-half by five centimetres in dimensions was made into a small roll wrapped about with fine silk thread by a number of turns and placed in the depth of the wound between the nerve and tendon. Nine days later the wound was reopened, and, while granulation and organizing tissue was plentiful, no Cargile membrane was found, not even the roll mentioned above, but the rolled-up silk ligature was easily found. Evidently the membrane had all been dissolved.

EXPERIMENT No. XVII.—The right tendo-Achillis and right posterior tibial nerve were exposed and wrapped separately with two turns of unchromicized Cargile membrane. The left side was treated in like manner, and the wound closed. On the fifty-fourth day after operation the dog was killed and each tendon and nerve was resected and examined. With the exception of a very small amount of scar tissue about the tendons and nerves, they appeared normal. No Cargile membrane was seen. Specimens were submitted to Dr. Ellis.

EXPERIMENT No. XVIII was a futile attempt to determine whether or not Cargile membrane could be made to replace, with any degree of efficiency, the dura mater. The temporal muscles of a dog having been turned down from the side of the head, the skull was opened by trephining. It was intended to remove a portion of the dura and replace it with Cargile membrane. Hæmorrhage, however, was copious, and I contented myself with rolling up a piece of unchromicized Cargile membrane three by four centimetres in dimensions, making a roll the size of a probe. This was wrapped about with several turns of fine silk suture to retain the form, in the hope that I might identify it when again sought. It was simply placed under the flap of temporal muscles to determine the action of the body juices. The wound, however, suppurated and vitiated the experiment, and the membrane was not again seen.

EXPERIMENT No. XIX.—A dog's temporal muscles having been turned down, the skull was trephined, and by means of rongeur forceps an opening in the skull two by three centimetres in dimensions was made, a piece of dura one by two centimetres was turned back and resected. This was replaced by a piece of chromicized Cargile membrane, the edges being slipped well under the dura throughout the entire periphery. A suppurating wound vitiated the experiment; but the resistance of the membrane is shown from the fact that, when removed thirty days later, the membrane was still intact, though porous and brittle. It was submitted to Dr. Ellis.

Two other operations were performed to determine, if possible, the efficacy, if any, of Cargile membrane in the cranial cavity. My results, on the whole, were bad; infection, as a rule, vitiated the experiments, and only the four were tried.

Judging from my work, however, I am inclined to believe from the frailty of the membrane and the difficulty of the handling it, except in the dry state, that the unchromicized variety is without value in cerebral surgery. I am inclined to think better of the chromicized membrane for this purpose. It is much more easily handled in the presence of a moist surface, and is not absorbed for a much longer period.

This completed the series of experiments so far as they seemed of value for the purpose of record.

My estimate of the value of Cargile membrane in preventing adhesions in the situations under consideration is embodied in our joint conclusions at the end of the article.

I avail myself of this opportunity to express my gratitude to Professor Coplin for his interest in this research, and for invaluable laboratory materials placed at my disposal; to Professors Keen and Da Costa for valuable suggestions and material aid; and to senior students C. C. White, L. F. Milliken, and Richard F. Taylor for assistance in the operative work.

HISTOLOGIC STUDY BY DR. ELLIS.

My part in this investigation consisted in studying histologically a number of specimens obtained at operation or autopsy by Dr. Craig. The tissues were fixed in Heidenhain's or Bensley's fluid and finally embedded in paraffin. Sections were stained by hæmatoxylin with the addition of eosin or Van Gieson, Mallory's reticulum stain, polychrome methylene blue, and Weigert's stain for elastic tissue. Those stained by hæmatoxylin and Van Gieson were the most satisfactory for purposes of study. I am deeply indebted to Professor W. M. L. Coplin for advice and assistance during the progress of the work. The description can best be taken up seriatim as the specimens were obtained and according to the experiment numbers of Dr. Craig.

The first specimen studied was a piece of unused Cargile membrane, sections of which were mounted and stained to obtain a basis of comparison for that in the tissues. The infiltrated mem-

brane is very brittle, and in many of the sections is broken into numerous fragments. This must be borne in mind in interpreting the later findings; breaking alone cannot be considered as evidence of actual destruction by the tissues. The membrane elects fibrous tissue stains and by them is colored deeply. The larger part appears homogeneous, but in many areas the membrane seems to be made up of several layers which are intimately fused. For this reason they are not clearly differentiated, but are indistinctly outlined by slight differences in stain reaction. These differences are not sufficiently definite to warrant the assumption that in the preparation of the material it is actually formed by assembling several layers. The membrane contains neither demonstrable cells nor cell nuclei.

EXPERIMENT II.—Intestine on which was placed Cargile membrane under four different conditions; specimen removed at end of fourteen days. A. Peritoneum denuded; chromicized Cargile. Over the operated area the peritoneum and longitudinal muscle are lacking. On the surface of the circular muscle and intimately connected with it is a layer of new fibrous tissue. At either margin of the denuded area, where the Cargile was folded upon itself, are from two to four layers of almost perfectly intact membrane. Between these layers, as well as separating them from the intestine, is new fibrous tissue. At both margins, beyond the Cargile, the omentum is firmly adherent. This new tissue also encloses the portions of the membrane still remaining. The whole area of adhesions thus appears to be surrounding and healing in the layers of membrane. Within the folds of the latter at one margin is a number of so-called foreign body giant cells, some of which are very large. The majority of these cells are in the new tissue at some distance from the membrane, but a certain number are directly upon it. Even where they are in contact with the Cargile, that material shows no evidence of degenerative action due to the cells, and phagocytic action by them is not demonstrable. Between the areas of adhesion at the margins of the denudation, Cargile is present only at some distance from the intestine, and there in the shape of short fragments that show some thinning. That it was broken by the knife in cutting may be inferred from the facts that the new fibrous tissue over the intestine beneath is firm and smooth, and that no adhesions of the omentum have formed. Sections lower in the block, from the

undenuded margin of the described area, show practically the same condition at the borders where adhesions have formed. Between these borders the appearance is also much the same, except that a narrow zone of very loose fibrous tissue is on the surface of the peritoneum; this zone is continuous externally with a band of dense new fibrous tissue similar to that over the denuded area. At points quite broad bands of new tissue extend from the peritoneum across the comparatively clear zone to the superficial layer, and thereby anchor it firmly to the intestine; this attachment of the new tissue, however, is not so intimate as in the case of the exposed muscle in the denuded area. Sections stained by polychrome blue show the presence of a very few cocci arranged singly and in pairs; morphologically they correspond to the ordinary pyogenic cocci.

B. Peritoneum denuded; unchromicized Cargile. The Cargile has essentially the same arrangement as in A. The folds at the margin of the denuded area are more fragmented, and the pieces show more disintegration than in the preceding instance. It is surrounded by the new tissue of omental adhesions. At one margin is the peritoneum and longitudinal muscle of a second coil of intestine that is firmly adherent at this point. Giant cells are not seen.

C. Peritoneum intact; chromicized Cargile. New fibrous tissue has formed on the surface of the peritoneum. The latter structure is dissociated, and through it the new tissue is extending into the outer muscle layer, where it substitutes certain of the fibres. As in the two preceding instances, there are dense omental adhesions beyond the margins of the membrane, and they extend inward and enclose the folds of that material. It is fragmented, conspicuously so between the adhesions where omentum is absent, but otherwise is fairly well preserved.

D. Peritoneum intact; unchromicized Cargile. This specimen is essentially the same as C, in which chromicized membrane was used. The membrane is slightly more frayed on the margins. Where the omental adhesions have formed and included the Cargile, the underlying peritoneum, as such, is no longer clearly demonstrable because of its disruption and intimate association with the new tissue.

EXPERIMENT IV.—Intestine on which was placed Cargile membrane under four different conditions; specimen removed at

end of four days. A. Peritoneum intact; chromicized Cargile. On the surface of the peritoneum of half the circumference of the intestine is a layer of formative tissue covered by fibrin in which is entangled a great many red blood-cells. At some points are numerous polynuclear leucocytes. The peritoneum is infiltrated with leucocytes which also invade the longitudinal muscle. Slight suppuration has occurred on the surface of the exudate as shown by many irregular spaces in the fibrin net-work, some of which contain granular detritus and polynuclear leucocytes. External to the exudate and not intimately attached to it is the Cargile, which is present on the borders of the involved area only, the middle half having almost or entirely disappeared. The appearance of the specimen and comparison of it with similar tissues indicate that the Cargile over the central portion disappeared mechanically during preparation or cutting of the tissue. That part which is present is broken into long pieces, but otherwise is intact. The exudate beneath the membrane and that included in the free central area are identical in structure. There is no evidence of adhesions of any kind.

B. Peritoneum denuded; chromicized Cargile. The peritoneum and longitudinal muscle are lacking. Over the denuded area is a fibrinocellular exudate in which organization is beginning, fibroblastic tissue being present on the surface of the circular muscle, which is infiltrated with leucocytes. Over this exudate is Cargile, which is intact throughout. There is no exudate external to the membrane and no signs of adhesions. Sections from a second block of this specimen are from the undenuded margin of the described area. They differ but little from the denuded space. Organization of the exudate is slightly further advanced. The Cargile over the denuded and undenuded areas presents the same appearance. Sections stained for elastica show none in the newly formed tissue; that in the vessels of the intestine is unchanged.

C. Peritoneum intact; unchromicized Cargile. An exudate composed of fibrin and polynuclear leucocytes is on the surface of the peritoneum, which is also infiltrated with these cells. Organization is beginning in the deeper layers, where vascularized tissue has already formed. The Cargile membrane has entirely disappeared. No adhesions have formed. Giant cells are not present. Sections appropriately stained show the presence of a

very few cocci differing in no way from the ordinary pyogenic types.

D. Peritoneum denuded; unchromicized Cargile. The peritoneum and longitudinal muscle are lacking. The circular muscle is infiltrated with leucocytes. On the surface is a thin layer of vascularized organizing exudate which is surmounted by numerous wavy fibrils of Cargile, appearing as if several sheets of the membrane had split a number of times and the layers had then broken into short fragments. Into the inner portion of this mass of membrane the formative tissue is extending. External to the membrane, for a part of its extent, are fibrin and polynuclear leucocytes. Covering the remainder of the Cargile and also surmounting the fibrinous exudate is a second layer of organizing tissue arising from the omentum, which here is closely adherent (Fig. 1). The serous covering of the omentum is disrupted, and the new tissue extends through it and for some distance into the underlying adiposa. At several points where formative tissue approaches the dissociated Cargile from both sides, the fibroblasts extend directly through the mass of fragments, forming continuous bands which at either end are vascular and becoming distinctly fibrous in character (Fig. 2). Sections from a second block of this specimen are from the undenuded margin. With the exception that the intestinal coats are intact, though infiltrated with the leucocytes, there is no essential difference from the denuded area. The adhesion of the omentum is the same as described when considering the preceding sections. In sections stained by polychrome blue, there are seen in the exudate moderate numbers of cocci arranged singly and in pairs.

EXPERIMENT VII.—Intestine of dog from which peritoneum was denuded and Cargile membrane applied; specimen removed at end of three days. Under the microscope, as macroscopically, no membrane is to be seen. The peritoneum is lacking over a considerable area, and, except at the extreme margins, the longitudinal muscle also has been removed. The central part of this denuded area is covered by a thick layer of exudate which is mainly fibrin, but also contains a few leucocytes, both mono- and polynuclear. This fibrinous exudate extends into the circular muscle, separating many of the superficial fibres. Beyond this, for more than half its breadth, the muscle is infiltrated with leucocytes, mainly polynuclears. Near the margin of the denuded

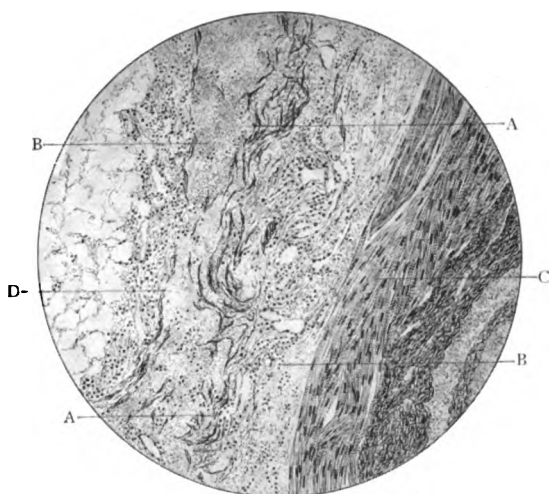


FIG. 1.—Intestine denuded of peritoneum and covered with non-chronicized Cargile membrane. Appearance at end of four days. (B. and L. $\frac{2}{3}$ obj., 1 inch ocular.)

A A. Fibrillated and fragmented remains of the Cargile membrane.

B B. Organizing exudate on either side of the membrane. That on the left, especially in the upper part of the field, is still largely fibrinous.

C. Circular muscle of the intestine; at this point the longitudinal muscle was removed during denudation. To the right are the submucosa and basement membrane.

D. Disrupted serosa of the adherent omentum.



FIG. 2.—From the same section as Fig. 1. (B. and L. $\frac{1}{6}$ obj., 1 inch ocular.)

A A. Fragments of the disintegrating Cargile membrane.

B B. Organizing tissue on either side of the membrane. That to the right is on the surface of the intestine; that to the left, on the surface of the adherent omentum.

C. Capillary blood-vessel in the new tissue.

D D. Two areas in which fibroblasts from either side have met through the fragmented membrane, thereby forming bands of adhesion.

area is a great deal of blood. The longitudinal muscle as it appears on the margin is densely infiltrated with leucocytes, and also contains numerous red blood-cells. Blood-vessels of the musculature are distended and contain an excess of leucocytes. The muscle fibres show varying degrees of atrophy. The fibrinous exudate extends for some distance over the peritoneum on either side of the denuded area, gradually thinning as the distance becomes greater. The sections are perfectly free from adhesions to omentum or other surrounding tissue.

EXPERIMENT VIII.—Intestine from which peritoneum was denuded and covered with Cargile membrane, which in turn was covered by rubber dam; specimen removed at end of three days. Microscopic examination of the denuded area shows absence of the peritoneum and essentially all of the longitudinal muscle. On the surface of the circular muscle is a thick layer of exudate which is mainly red blood-cells, but also contains some fibrin and a few leucocytes. This extends into the muscle and separates many of the superficial fibres. The blood-vessels of the muscle are distended, and the inference is that from them hæmorrhage has occurred. Surmounting this mass of blood is a layer of Cargile membrane, which for a small part of its extent, at one end, is perfectly intact. Throughout the greater part of its length it has undergone more or less marked disintegrative changes. It is split into numerous thin layers or fibrils, and these are broken into pieces irregular in shape and of variable size, some being very small. The fragments are widely separated, occupying a space many times as broad as the normal Cargile. Between and surrounding these fragments is the exudate. External to the membrane is a layer of exudate nearly as thick as that between the membrane and the intestine, but differing greatly from it in constitution. The former is made up almost wholly of fibrin and polynuclear leucocytes, very few red blood-cells being present. Leucocytes are exceedingly numerous, and both they and the fibrin show some necrosis. At the point where the Cargile is intact, there is a very sharp differentiation between this external layer of fibrinocellular exudate and the blood beneath the membrane. Where the Cargile is disintegrating, the blood has passed through and permeated for some little distance the exudate externally; the polynuclear leucocytes of the latter have in turn penetrated the blood-clot, this admixture through the partially destroyed mem-

brane being very conspicuous. Polynuclear leucocytes are at many points in direct contact with the fragments of Cargile, but there is no evidence of special disintegration at those places. Phagocytosis is not demonstrable.

EXPERIMENT IX.—Fold of chromicized Cargile membrane that was enclosed in a perforated glass tube and placed in peritoneal cavity; tube removed at end of two weeks. A small amount of reddish-colored material adhered to the end of the tube near the largest opening. Under the microscope this is shown to be made up of red blood-cells and leucocytes, the latter ten times as numerous as the former and mainly polynuclear in type. Eosinophiles are not in greater proportion to other leucocytes than in normal blood. On section, the Cargile is found folded in many layers. The membrane is slightly thicker than normal, or when placed on tissue, and appears to be swollen, possibly by the imbibition of fluid. This appearance is further heightened by lessened density, as shown by the staining reaction and also by roughening or slight fraying of the surfaces. The membrane, however, is intact throughout. Between the layers are masses of partly disintegrated red blood-cells and numerous leucocytes, mainly polynuclear in type.

EXPERIMENT X.—Intestine denuded of peritoneum and covered by Cargile membrane, the latter being covered by rubber dam; specimen removed at end of six days. The peritoneum and longitudinal muscle are lacking. On the surface of the circular muscle is a thick layer of organizing exudate, the most advanced portions of which, bordering the muscle, are just assuming the characters of fibrous tissue; external to this is a well-marked zone of vascularized tissue, and on the surface a layer of fibrin and polynuclear leucocytes. The circular muscle also shows leucocytic invasion. In the fibrinous exudate at one point are a few fragments of Cargile membrane, the remainder having entirely disappeared.

EXPERIMENT XI.—Cargile membrane from a sealed celloidin capsule that was in the peritoneal cavity for seven days. The membrane is very much swollen, most of it being more than twice the normal thickness. The margins are decidedly frayed, presenting at some points a serrated appearance. Although the sections are very thick, the density is much lessened, many areas being semi-translucent; at points are small clear spaces or open-

ings. Stains are taken with much less avidity than by the other specimens of the membrane studied. No cells are present. The appearance of this specimen is strongly indicative that the membrane is undergoing slow absorptive changes.

EXPERIMENT XII.—Cargile membrane and fluid from celloidin capsule that had been in peritoneal cavity thirty days. This specimen was first examined by Dr. Coplin, who kindly furnished the following description: "The capsule is surrounded by what appears to be fibro-fatty tissue, presumably a part of the omentum. Around the irregular and slightly rough end of the capsule, that had been closed by ligature and sealing, the tissue attains a thickness of two to five millimetres. Towards the opposite or smooth end of the capsule the enveloping tissue hardly exceeds one millimetre, and at points is so thin that it is quite transparent. After incision of the soft tissue the capsule readily slipped out. Along one side it is dark in color, and in places is slightly wrinkled. It is evident there is fluid within, but it escapes at no point, even when gentle pressure is made upon the capsule. Upon opening the latter, the contained fluid is found to be of about the consistency of blood serum, slightly opalescent, possessing a faint pink tinge, decidedly cloudy, and containing scarcely perceptible irregular granules to which the cloudiness appears to be due. This fluid was examined in the fresh condition, also stained by Sudan III, methylene blue alone, and with eosin, and by Wright's stain. It is found to contain large quantities of granular material of a form usually characterized as cellular detritus. Some of the granules are grouped, and occasionally small, stringy granular bodies are observed. The granules vary in dimensions from one to four or five microns, and in some fields are collected into masses 100 or more microns in diameter. The larger number of granules are strongly acidophilic. With them are numerous spherical bodies possessing the general appearance of fat droplets and taking Sudan III strongly. Occasionally one sees what, by stretching the imagination, may be thought to resemble a shrunken cell of some kind; such bodies, however, are extremely rare. No structures resembling leucocytes or bodies corresponding to any histological structure can be identified. By proper staining methods, bacilli two microns in length and less than one micron in width are seen to be fairly abundant. These bodies could be recognized in unstained specimens, and were not motile. Cocci of ordinary

dimensions, indistinguishable from usual pyogenic organisms of this group, are occasionally observed; they are not, however, in masses, nor are they abundant. The bacilli are far more numerous. The bacteria were not identified. The capsule also contains an extremely thin membrane-like structure, the dimensions of which are not determined." Later examination of this structure left little doubt that it was the much thinned Cargile membrane. It was left in salt solution for some hours; at the end of that time the salt solution was very turbid and the membrane had entirely disintegrated and disappeared. The value of this experiment, undertaken to determine the effect upon Cargile membrane of body fluids without the presence of cells, was vitiated by the occurrence of infection, and deductions therefore must be restricted.

The new tissue which had formed around the capsule is a band of varying breadth, the external portion of which is quite dense, newly formed fibrous tissue. Firmly adherent to three-fourths of the circumference is normal appearing adipose tissue. Towards the inner surface of the band, the fibrous tissue is less dense, and contains more cells. On this surface at points are leucocytes, both mono- and polynuclear in type. At other places, or along with the cells, is considerable fibrin. Both cells and fibrin show evidence of slight necrosis.

EXPERIMENT XIII.—Posterior tibial nerve which was isolated and wrapped with Cargile membrane; specimen removed at end of fourteen days. A. Nerve from left side, covered with four layers of unchromicized Cargile. Sections from one block of this specimen show between the nerve trunk and the fibrous tissue which half surrounds it the layers of the membrane. Of the four layers, the outer two, or those in contact with the tissues on either side, are intact, or nearly so. The two inner layers are not so well preserved. All four are separated some distance from each other in the wide space between the nerve and the enclosing tissue. The outer layers are partly enclosed by polyblasts or by recent fibrous tissue. This extends through the small breaks that are present in the membrane. Organizing tissue is also found between the layers of the membrane, but is not so prominent around the two inner as is that enclosing the two outer. No distinct adhesions are present in this section, the newly forming fibrous tissue on the two sides apparently being prevented by the membrane from

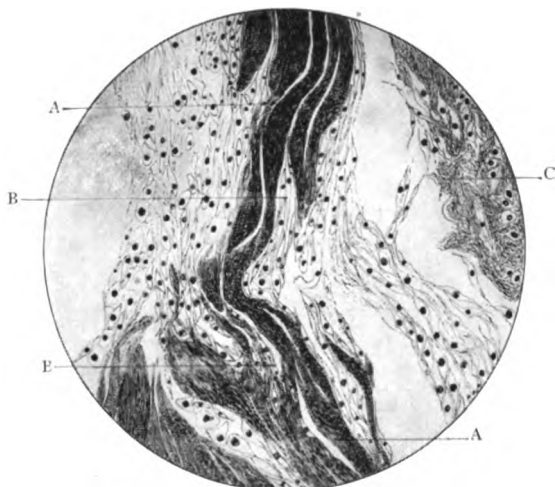


FIG. 3.—Layer of non-chronicized Cargile membrane surrounding posterior tibial nerve for fourteen days. (B. and L., $\frac{1}{2}$ homo. imm., 1 inch ocular.)

A A. Cargile membrane splitting into fibrils, but otherwise fairly well preserved.
B B. Spindle-shaped fibroblasts which are entering between the fibrils of the membrane. The appearance at and below the lower letter indicates that there is an intimate connection between the splitting of the Cargile and the intercalation of the formative cells.
C. New fibrous tissue internal to the membrane.

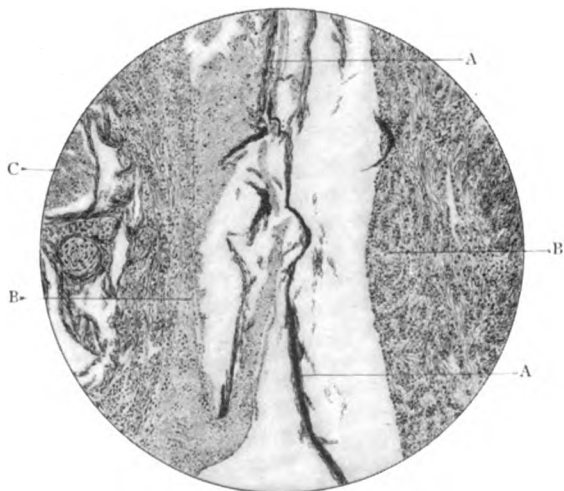


FIG. 4.—Three layers of chronicized Cargile membrane surrounding posterior tibial nerve for fourteen days. (B. and L., $\frac{2}{3}$ obj., 1 inch ocular.)

A A.—Cargile membrane. Two layers and a few isolated fragments of the third are still present. Varying degrees of fibrillation and fragmentation are shown.

B B. Newly formed or forming fibrous tissue bordering the space containing the Cargile. That on the right surmounts the connective tissue separated from the nerve when the membrane was placed; on the comparatively smooth border repair is sufficiently advanced probably to be beyond the adhesive stage. The new tissue on the left, surrounding the isolated nerve, is not so far advanced; on the surface and extending between the layers of the membrane is fibrinous exudate containing a few leucocytes.

C. Part of a nerve bundle immediately beneath the new tissue. Degenerative changes have rendered this portion of the nerve almost unrecognizable.

uniting. A few giant cells are in the new tissue surrounding the nerve. One large one with six nuclei has in it a fragment of fibrous tissue that is roughened, and appears not unlike equal-sized pieces of Cargile membrane as it is found elsewhere. From the fact that these are typical "foreign body" giant cells developed only in the neighborhood of the membrane, it is reasonable to suppose the Cargile is the origin of the fragment in question. Whether or not this be an instance of phagocytic destruction and removal of the membrane, it is the only suggestion of such process found in the entire series of specimens. The membrane in those areas where reparative processes are most active is splitting into fibrils, and between them polyblasts and spindle-shaped fibroblasts are insinuating their way (Fig. 3). In this manner the membrane appears to be disrupted and removed, or finally incorporated with the new tissue. Sections from another block of this specimen show the new fibrous tissue more prominently; at one point is a continuous band joining the two sides, though it extends in an irregular and zigzag manner among the fragments of Cargile. The appearance of the entire section is that uniform adhesions will finally result. A few giant cells are present, but they are not large, and are not in direct contact with the membrane.

B. Nerve from right side, covered with three layers of chromicized Cargile. Two layers of Cargile extend entirely around the nerve, except where broken in cutting or by destructive action of the tissues. Within these, directly upon the nerve, is a band of forming fibrous tissue, upon the surface of which is a fibrinous exudate containing many red blood-cells; this exudate is for the most part in contact with the Cargile. The areolar connective tissue, which was separated from the nerve when the Cargile was placed, is also covered by a layer of new tissue which is smooth and sharply limited as though repair was complete; it is nowhere penetrating or adherent to the membrane in the sections from A (Fig. 4). No giant cells are seen. Sections from another block of this specimen show new tissue advancing between the layers of Cargile, but no adhesions have formed.

EXPERIMENT XIV.—Tendo-Achillis and posterior tibial nerve. Two layers of Cargile around tendon, nerve not covered; specimen removed at end of twenty days. Cargile can be identified over approximately three-fourths of the circumference of the tendon. It is split into several thin layers and broken into short

fragments. Throughout the entire extent, where visible, it is enclosed in a narrow space bounded by dense, newly formed fibrous tissue. For a part of the distance it is partially free in this space, which also contains red blood-cells. In such areas actual adhesions do not appear to have formed. At irregular intervals, however, fibrous bands unite the tissue on either side, and the Cargile is thus incorporated in a nearly healed wound; at many of these points the membrane has essentially lost its identity as a distinct structure. In several areas are numerous foreign body giant cells nested in small spaces, which they entirely fill or they are surrounded by loose areolar tissue. From these areas the Cargile has entirely disappeared. Phagocytosis by these cells is not demonstrable. In the fourth of the circumference where Cargile is entirely absent is a solid band of fibrous tissue, giving the impression that the membrane had not been present over this area.

EXPERIMENT XVII.—Tendo-Achillis and posterior tibial nerve. These were separated and each covered with Cargile membrane; specimen removed at the end of fifty-four days. In sections from this specimen can be found no evidence whatever of the membrane or the place formerly occupied by it. There appears to be but little excess of fibrous tissue over that which would normally be found in this location. At one point is a small circumscribed area made up almost entirely of giant cells surrounding fragments of a suture.

EXPERIMENT XIX.—Chromicized Cargile membrane from brain of dog; specimen removed at end of thirty days. This specimen is very brittle when mounted. Sections show that portions are of normal density, but slightly thinned. Still other parts are thickened, spongy in character, and stain less deeply than usual. The total bulk of the membrane appears to be slightly less than for normal membrane of the same extent; the loss, however, is not conspicuous.

The object of these histologic studies was to determine, if possible, the fate of Cargile membrane in the tissues, and also its effect upon those tissues it was intended to protect. The major portion of the findings has been embodied in our conclusions, but one point seems worthy of special emphasis. The irritative action of the membrane as a foreign body,

especially in the peritoneal cavity, is so pronounced that it cannot be disregarded, and appears to be the principal factor militating against the otherwise beneficent possibilities of the material. In the case of raw surfaces it is difficult to estimate this action, but in every instance in which the membrane was placed over intact peritoneum, reactionary new tissue formed on the surface of the latter, which in many cases was disrupted and incorporated with the new formation. When the membrane is placed between two freshly incised surfaces, this stimulus towards "healing in" of the foreign material is added to the reparative efforts common to all wounds, and their resultant action must be withstood if adhesions are prevented. It does not appear that Cargile membrane is able so to do.

Our joint conclusions are:

1. The most distant time at which we found unchromicized Cargile membrane existing intact, macroscopically, within the peritoneal cavity, was the fourteenth day; in most instances it had disappeared to macroscopic view much sooner. The earliest time at which we found the membrane had disappeared over the area of actual denudation was on the third day.

2. Unchromicized Cargile membrane when buried in living animal tissue, as when placed around tendons and nerves, or in muscle, is apparently absorbed sooner than when placed within the peritoneal cavity. In no instance was so much as a fragment of the membrane observed macroscopically so late as the fifth day, though in the fragmental state membrane was noted microscopically so late as the fourteenth day.

3. Chromicized Cargile membrane when placed within the peritoneal cavity or when buried in living animal tissue remains unabsorbed much longer than does the unchromicized variety. The two varieties doubtless bear relatively the same relation to each other, so far as absorbability is concerned, as do chromicized and unchromicized catgut.

4. While the unchromicized, and to a less extent the chromicized, variety will adhere fairly firmly to a surface denuded of peritoneum when such surface is relatively dry, yet neither can be depended upon to remain where placed, unless

anchored by some method, in a situation which is subject to peristaltic activity.

5. A logical deduction from the results of the foregoing experiments seems to warrant the belief that neither variety of the membrane is of value in preventing adhesions within the peritoneal cavity. In every instance the membrane, until absorbed, appeared to act as a foreign body, and therefore as an irritant.

6. We believe from the results of our observations that both varieties of the membrane are of value in preventing adhesions to wounded nerves and tendons when such structures lie in tissues which have been subjected to trauma, operative or otherwise. Our conviction is that for this purpose the chromicized is the more valuable.

7. We believe that several layers of either variety of the membrane when placed around tendons or nerves afford a safer and better protection than one layer.

8. We believe that, when used in the cranial cavity to replace destroyed or removed dura, the unchromicized variety would be exceedingly difficult to handle on account of its being unmanageable when moist; and we further believe, on account of the rapidity with which it dissolves, that it would be of no special value in this situation even though it could be used with ease. Owing to the facility with which the chromicized variety can be handled, its greater toughness and increased power to resist absorption, we believe that it would prove of greater value in replacing the dura.

9. Our studies indicate that the membrane is destroyed by a lytic substance, or substances, contained in the body fluid. The celloidin capsule experiments, even though bacteria were present in one, show that the membrane is softened, and at least partially absorbed by body fluids without the presence of cells. In the tissues it is split into fibrils, this change being accompanied or followed by the penetration of formative cells of the new tissue enclosing it. Fragmentation, disintegration, and absorption finally ensue. Phagocytosis may safely be excluded as a chief important contributing cause.

A CASE OF ACUTE LYMPHATIC LEUKÆMIA.

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At the beginning of the nineteenth century pallor of the blood, as if mixed with pus, was observed by Bichat. This appearance combined with enlargement of the spleen was observed by Velpeau¹ in 1827. The alteration in the blood depending on an excess of leukocytes Donne described and interpreted in 1844 as due to imperfect transformation of white into red blood cells.

In October, 1845, Hughes Bennett and Dr. Craigie² published two cases of the disease, and to the former appears to belong the credit of recognizing the salient features of the affection as a distinct malady. In November, 1845, Virchow³ published another case independently and admirably worked out.

In all these cases the change in the blood was only recognized after death. Virchow proposed the name leukæmia and Bennett leukocythemia. It was first observed during life by Dr. H. M. Fuller in 1846 and subsequently by Dr. Walshe.

In 1848 the first case during life was diagnosed by Vogel. Ebstein,⁴ in reporting several cases, calls attention to the fact that traumatism may play an important role in the etiology. A. Fraenkel,⁵ in organs from a case of leukæmia, pointed out that there was present a lymphoid infiltration, especially of the kidney. Herman Suchannek⁶ found in the nasal mucous membrane that the olfactory epithelium was normal, but that the glandular structure was destroyed by the infiltration of lymphocytes. Monroe⁷ cites a case of leukæmia in which there were found on histological examination numerous small oval bodies in the heart, between the fibres, smaller than nuclei of leukocytes, and too irregular in size to be regarded as bacteria. They were not present in any other organ. Grewe⁸ reports a case of acute lymphatic leukæmia following a strain in lifting a weight, in which the blood was characteristic of lymphatic leukæmia. At autopsy, the lymph glands were enlarged, spleen hypertrophied, and the liver and kidneys contained lymphoid nodules. Palma⁹ reports a case of primary sarcoma of the thymus with secondary deposits in the lymph glands. A month later the patient showed an increase in the number of leukocytes and Palma

concluded it to be a case of lymphatic leukæmia preceded by pseudo-leukæmia. Dock¹⁰ mentions a case of chloroma, which condition was most marked in the periosteum in and about the orbit, and numerous widespread metastatic nodules, all of a pea-green color. The polynuclear leukocytes averaged 20 per cent., the small lymphocytes 7 per cent., and the large lymphocytes 65 per cent. Normoblasts occurred in the proportion of two to five per thousand of red corpuscles. Only one eosinophile could be found "out of many thousand leukocytes counted."

Fraenkel believed that the large lymphocytes could be regarded as pathognomonic of acute lymphatic leukæmia. Hirschloff reported two cases of leukæmia in which most of the leukocytes were large mononuclear cells without granules; some, however, contained neutrophilic and some eosinophilic granules. According to Birch-Hirschfeld and Benda the variation in size may have an anatomical basis in the hyperplastic lymph nodes, as in some cases these contain mostly small lymphocytes. Müller claims that myelocytes (both neutrophilic and eosinophilic) and mast-cells are usually absent or extremely scarce in leukæmia. Polynuclear leukocytes (both neutrophilic and eosinophilic) are also comparatively scarce. Nucleated reds are usually very scanty and may not be found at all, according to Ewing.¹¹ Intercurrent affections may greatly alter the appearance of the blood in leukæmia. Fraenkel cites a case in which the leukocytes fell from 220,000 to 1200, and ascribes it to a pure leukocytolysis. After typhoid fever, pneumonia, empyema, erysipelas, septicæmia, tuberculosis, and carcinoma the same changes have been noted.

Kraus recently reported a case in which the leukocytes fell from 393,000 to 4000 as the result of double pneumonia and empyema. The viscera showed no evidence of leukæmic infiltration and he inferred that the infection had not only transformed the blood, but had resolved the essential visceral lesions as well.

After the subsidence of the infection, the blood soon resumes its original condition, according to Grawitz. The reduction of leukocytes can also be accomplished by experiment, as in a case cited by Jacob, which showed 850,000 reduced to 282,000 by the injection of glycerin extract of spleen. Richter obtained the same results by injecting spermin; and Henck¹² by injection of tuberculin. Kinnicutt¹³ reports a large number of eosinophiles in the blood in a case of leukæmia. Nobl¹⁴ regards the mitoses of Müller as the only certain evidence of leukæmia. In two cases examined the eosinophiles were scanty. In Uthemann's¹⁵ case 93 per cent. of the white cells were lymphocytes. According to Osler¹⁶ eosinophiles and nucleated red corpuscles are rare and myelocytes are not present. Cafafy¹⁷ claims that the amoeboid movement of the white cells is feeble, due in all probability to the large number of mononuclear elements present. Of 16 cases of leukæmia reported by A. E. Taylor,¹⁸ 12 presented an increase in the number and percentage

of mast-cells. In the remaining 4 cases no mast-cells were demonstrable. He stated that not one of the cases showed 4,000,000 red cells, and claimed that there was always an oligocythæmia present. He considers the condition to be due either to cachectic or nutritional disturbances, to toxic hemolysis, or to disturbances in the bone-marrow. Polychromatophilia and poikilocytosis are almost constant features in leukæmia. Nucleated red cells, most of which were normoblasts, were found in all but one case of the sixteen examined. Microblasts, macroblasts, and poikiloblasts were also present. The lymphocytes were devoid of movement, while the myelocytes showed constantly slight motility. As low a percentage as 15.6 of polymorphonuclear leukocytes was noticed in one case. Eosinophilia was not constantly present in lymphatic leukæmia, while it was invariably present in myelogenous leukæmia. Leukoblasts, according to Löwit, can be found in developmental areas in the lymph glands, spleen, intestines and bone-marrow in acute leukæmia. In but one case of lymphatic leukæmia were circulating mast-cells demonstrable. Fraenkel admits that myelocytes may occur in acute lymphatic leukæmia, and Benda claims they are frequently, if not constantly, found in the circulating blood and that local basophilia is very common in leukæmia.

Dunn¹⁹ cites leukæmia in a child of eight years, in which there was a crescentic tumor in each upper eyelid. The first evidence of the disease was a swelling in the parotid gland, which increased greatly in size and became as hard as stone.

Middleton²⁰ contributes 2 cases of leukæmia, one a child of sixteen months, the other a boy four years old. In the first the proportion of leukocytes to erythrocytes was 1 to 9. Paris²¹ cites a case of leukæmia in a boy of seventeen years which after six days terminated fatally. Post-mortem examination showed the typical lesions of leukæmia in the spleen and liver, but the lymphatic glands were wholly normal. Eichhorst²² also mentions acute leukæmia in a lad of eight years; the duration of the disease, fourteen days.

Vesemeyer²³ reports 3 cases of acute leukæmia terminating in three, five, and ten days, respectively; Ortnier,²⁴ a child eight and a half months old, and Ebstein²⁵ reports a case ending fatally six weeks after the patient first came under observation. Ord and Copeman²⁶ call attention to a case of five years' standing; Lannois²⁷ one of three years' duration.

Saenger²⁸ records the occurrence of lymphatic leukæmia in a pregnant woman in which premature labor had to be induced on account of unbearable distention from uterus and spleen. He also calls attention to a case of congenital leukæmia, the child being stillborn in the thirty-second week. The blood upon examination showed one white to three red blood cells. The mother's blood was not examined. Litten²⁹ reports acute lymphatic leukæmia following influenza that terminated in three days; Guttman, a

child of ten years, in which the ratio of white to red cells was 1 to $1\frac{1}{2}$, and that only a single eosinophile was observed in a preparation; Wertheim, in a case of lymphatic leukæmia, found no nucleated reds, the white corpuscles numbering 480,000. Thayer³⁰ mentions that nucleated red cells are rare, and if present are likely to be megaloblasts. Müller found very few eosinophiles in a case of lymphæmia; Thayer³¹ found 0.1 per cent.

Wilkinson³² reported a case of leukæmia which, upon first examination of the blood, showed 560,000 leukocytes, chiefly myelocytes. Eight days later a second examination was made, when it presented all the features of lymphatic leukæmia, while only an occasional myelocyte was observed. Nucleated red cells—normoblasts and megaloblasts—were present, the latter predominating. At the first examination of the blood so much polymorphism of the white cells existed that an accurate differential count could not be made. No necropsy was obtained.

Nichols³³ reports 2 cases of acute lymphatic leukæmia. In one the leukocytes numbered 67,800 per c.mm., "all of which excepting a small proportion were large lymphocytes." A second examination made three days later showed 134,800 leukocytes per c.mm., in which the large lymphocytes numbered 91.3 per cent. and small lymphocytes 7 per cent. In this case a coccus was present "differing from the ordinary known cocci" in the blood and organs, but produced no specific action when inoculated into guinea-pigs and rabbits. In another case the leukocytes numbered 529,000 per c.mm. Eighty-five per cent. of them were large lymphocytes, 10 per cent. small lymphocytes.

A. O. J. Kelly³⁴ cited 4 cases of acute lymphatic leukæmia. The first showed 17,000 to 30,000 leukocytes, 93 per cent. of which were lymphocytes; the second (a young woman who had been delivered of a child a short time before), where the leukocytes ranged from 200,000 to 400,000 and the lymphocytes constituting 98 per cent.; the third, a young man in whom sepsis was suspected, a differential count of the blood showed 98 per cent. lymphocytes; the fourth, a man whose spleen was enlarged, where the leukocytes varied from 12,000 to 38,000.

Kelly doubts the non-identity of the two varieties of leukæmia—myelogenous and lymphatic. He bases his doubts upon several conclusions: 1. The occurrence of cases of so-called acute lymphatic leukæmia, with little or no enlargement of the lymph glands. 2. The demonstration of the predominance of lymphadenoid changes in the bone-marrow in every case of lymphatic leukæmia in which the bone-marrow has been examined—observed by Neumann many years ago. 3. The fact that distinctions between the lymphocytes and the granulocytes are of degree rather than of nature, since the lymphocytes are unquestionably amœboid, some possess granules in their protoplasm, and there is some evidence

of the occurrence of an active lymphocytosis. 4. The fact that the lymphocytes and the granulocytes (myelocytes and the granular cells of the circulating blood) develop from a common ancestor in the bone-marrow—at least, in pathological states. 5. The fact that even clinically there is no sharp dividing line between the two forms of the disease.

Rather than two forms of the disease, there are extremes of type. That atypical and transitional (intermediate or mixed) forms do occur, and while we have hitherto thought that acute leukæmia is always lymphocytic and chronic leukæmia either lymphocytic or myelocytic, trustworthy evidence has recently accumulated tending to show that acute leukæmia may be, though rarely, myelocytic. Contrary to the rule, certain of the chronic lymphocytic cases reveal a usually large number of large lymphocytes, and some of the apparently acute cases may be of the small lymphocyte type.

Fraenkel,³⁵ reporting 10 cases of acute leukæmia, “drew particular attention to the blood picture which he considered typical for such cases. He describes the predominating cell as varying greatly in size from that of a red blood corpuscle to those twice as large and showing every grade of transition between the two. The large cells contain voluminous nuclei which nearly fill the cell, leaving only a narrow zone of protoplasm about them. The nuclei are round or oval, but many show indentations, and some are even polymorphous. The typical small lymphocytes are much less numerous than these large elements, but are still absolutely increased above the normal. He notes further the absence of myelocytes and eosinophiles and the relative and even absolute decrease in the number of polymorphonuclear neutrophiles.”

Hamman³⁶ reports 3 cases of acute leukæmia in which there was an increase in the large mononuclear cells (hyaline(?) cells).

The counts of the leukocytes were in the first case 111,000, of which 77 per cent. were large mononuclear cells; in the second 119,200, of which an average of 74.4 per cent. were large mononuclears in two counts, while in the third there were 958,000 leukocytes with 90 per cent. large mononuclears. He claims that it appears unjust from the evidence at hand to relegate a blood picture as distinctive as that of Fraenkel to a subgroup under the lymphocytic variety.

In the absence of any definite pathological basis our only means of classifying leukæmias is according to the blood picture. Ehrlich was the first to adopt this method, but he uses the blood picture merely as a gauge to certain anatomical seats of the disease. Evidence being in favor of the absence of such an indication, it has been proposed to replace the terms myelogenous and lymphatic by the more uncompromising ones, myelocytic and lymphocytic, which have reference to the blood picture alone.

Savory,³⁷ in a child aged four and a half years, who presented enlarged glands of the axilla and above the right clavicle, found upon examining the blood 35 per cent. hæmoglobin, 2,157,000 red cells, and 356,000 leukocytes. Spreads of the blood stained with hæmatoxylin and eosin showed that the red cells were practically normal, and only found two nucleated red cells while counting 611 white cells. Both were normoblasts. A differential count of the leukocytes gave: polynuclears 3.45 per cent.; large and small lymphocytes, 96.07 per cent.; eosinophiles, 0.33 per cent.; myelocytes, 0.16 per cent. "The large lymphocytes greatly predominated, but there was no line of demarcation between the large and the small; so they were counted together. The majority seem about from 12 to 14 μ in diameter." Death occurred in seven weeks. No autopsy was performed.

Zypkin³⁸ reports a case of a woman, aged thirty-nine, in whom a first examination of the blood showed the presence of 2,700,000 erythrocytes, 8800 leukocytes, and 35 per cent. hæmoglobin. At this examination the polynuclear leukocytes were 64.5 per cent.; large lymphocytes, 22.4 per cent.; small lymphocytes, 5.4 per cent.; mononuclear leukocytes with ungranulated protoplasm, 6.4 per cent., and eosinophiles, 1.3 per cent.

Two weeks later the erythrocytes were 1,550,000; leukocytes, 106,400; hæmoglobin, 24 per cent. In this report the large lymphocytes were 64.7 per cent.; polynuclears, 11.9 per cent.; small lymphocytes, 6.3 per cent.; mononuclear neutrophiles, 2.4 per cent.; mononuclear leukocytes with ungranulated protoplasm, 14.4 per cent.; eosinophiles, 0.3 per cent. Poikilocytes, normoblasts, and megaloblasts were present. In this case there was enlargement of the spleen—four fingers' breadth—below the border of the ribs, and the observer thinks that it was primarily a splenic anæmia in which a transition into acute lymphatic leukæmia occurred.

G. S. Middleton³⁹ reports a case of acute lymphatic leukæmia occurring in a youth nineteen years of age which proved fatal three months after the glandular enlargement was first noticed (cervical glands). The white blood cells, though not counted in a hæmocytometer, were estimated at about 30,000 per c.mm. Large lymphocytes were 87.3 per cent.; small lymphocytes, 4.2 per cent.; polymorphonuclears, 2.5 per cent.; large mononuclears (hyaline), 6 per cent. No marrow-cells or mast-cells were observed and extremely few eosinophile cells. The red corpuscles showed a moderate poikilocytosis, but no nucleated reds were found. The number of erythrocytes and the percentage of hæmoglobin were not estimated.

Puchberger⁴⁰ claims that in leukæmia there are observed markedly hypertrophic forms of blood platelets, which sometimes attain the size of lymphocytes. When the blood is stained with brilliant cresylene blue he noticed, after the lapse of ten or fifteen minutes, the separation of a hyaline substance which, in the form of a cylin-

der, is inseparably attached to the similarly circumscribed stained substance of the blood platelet.

Wende⁴¹ mentions a very interesting case of lymphatic leukæmia preceded by Hodgkin's disease. There was spontaneous increase and reduction of tumors, characteristic of Hodgkin's disease, with suddenly developing clinical and blood changes showing transition from pseudoleukæmia into true lymphatic leukæmia. The first blood examination gave: hæmoglobin, 88 per cent.; erythrocytes, 5,128,000; leukocytes, 4000. Differential count: lymphocytes, small, 27 per cent.; lymphocytes, large and transitional, 4 per cent.; polynuclears, 68 per cent.; eosinophiles, 1 per cent. Microblasts and microcytes were occasionally observed.

Several months later two blood examinations gave a general result as follows: hæmoglobin, 40 per cent.; erythrocytes, 1,856,000; leukocytes, 39,000; lymphocytes, small, 95.4 per cent.; lymphocytes, large, 1.1 per cent.; eosinophiles, 0.5 per cent.; polynuclears, 2.9 per cent.; myelocytes, 0.1 per cent. Microcytes, macrocytes, and poikilocytes were observed, as well as an average of 168 nucleated reds (102 in first and 225 in second) per c.mm. and a number of polychromophiles.

A streptococcus infection occurred, and just twenty-four hours before death the hæmoglobin was 30 per cent.; erythrocytes, 803,000; leukocytes, 1600, and the specific gravity 1.030. Megalocytes and poikilocytes were found, together with schistocytes; no normoblasts. The small lymphocytes were 88 per cent.; large and transitional lymphocytes, 1 per cent.; polynuclear neutrophiles, 10 per cent.; eosinophiles, 1 per cent. Infiltration of lymphocytes was more or less marked in all the organs and in the skin.

Dorothy Reed⁴² cites a case of a man, aged forty-seven years, in whom the disease was preceded by a severe attack of epistaxis. The blood was examined twice, ten days and seven days before death. An enormous increase in the leukocytes was apparent, the white cells being about as numerous as the erythrocytes. No differential count was made. No general or even local enlargement of the lymphatic glands was noticed; the bronchial, peritracheal, and aortic glands, though deeply pigmented, were rather soft and translucent. The mesenteric glands were not enlarged, were deeply pigmented, grayish-yellow and translucent, and somewhat softer than normal. Along the retroperitoneal region the hæmolymp glands were very conspicuous, had a dull-red color, and were not especially enlarged.

In blood smears made from the heart at autopsy in over a thousand non-granular mononuclear cells, only three or four granular polynuclear leukocytes and four normoblasts were seen. The uninuclear cells varied from cells almost twice the size to those considerably smaller than the normal red blood cells. The nuclei were round or oval. The red cells appeared normal in size, form,

and staining properties. Nucleated cells were of the normoblast type. Section of a chicken-fat clot from the heart showed a mesh-work of fibrin and entangled leukocytes, the most conspicuous of which was the lymphoid cell. In the marrow the predominating white cell was the lymphocyte; few normoblasts, but no megablasts, were observed. In the lymphatic glands the sinuses were engorged with lymphocytes and the follicles to a less extent. All the viscera contained small foci of infiltration of lymphocytes, but none to a marked degree. Reed suggests that "there are three forms of leukæmia, all due to myelogenous changes, and that these should be known as the myelocytic, lymphoid, and mixed-cell varieties, if we wish to make the blood picture the basis for clinical divisions."

Miller and Hess⁴³ report a case of acute leukæmia with death due to rupture of the spleen. The leukocytes varied from 50,000 to 161,000. An average differential count gave: small lymphocytes, 4 per cent.; large lymphocytes, 81 per cent.; eosinophiles, 3 per cent.; myelocytes, 1.5 per cent., and polynuclears, 10.5 per cent. Numerous megaloblasts were observed.

Williams,⁴⁴ in speaking upon the pathology of leukæmia, claims that there are two forms: one in which the cells are derived from the marrow (myelocytic) and one in which the cells originate mainly in the lymph glands, though also found in smaller numbers in the spleen and marrow (lymphocytic). Lymphatic is a rarer disease than myelocytic leukæmia, and the primary affection is in the lymph glands. We find these glands enlarged, whitish or grayish-white on section, and overloaded with lymphocytes. Many are decidedly larger than usual, but all are of the same type. We never find any form of marrow cells or eosinophiles in pure lymphatic leukæmia. Secondary deposits of a similar character are regularly found in the spleen and marrow and sometimes in other organs. The blood is surcharged with lymphocytes, great and small. The primary disease—leukosis—is seated in the lymph glands.

Pawlowski⁴⁵ describes a bacillus in the blood and tissues, especially in the lymphatics and blood paths of the liver, in three cases of leukæmia. He infers that the leukæmia is the reaction of the leukocytes of the blood-forming organs and to a less extent of the blood itself to the irritant bacillus. Fermi isolated a short, blunt bacillus from the spleen of a person dead of leukæmia, but failed to find it in twelve spleens in persons dead of other diseases. Kelsch and Villard⁴⁶ found and proved the pathogenic properties of the bacillus (in rabbits) discovered by Fermi.

A. Westphal⁴⁷ reports a case of acute leukæmia in which death was precipitated by a puncture of the spleen made for diagnostic purposes. At the necropsy the spleen was enveloped with a large blood clot; no large vessels were ruptured. Cultures were made from all the internal organs and fluids with negative results.

Ord and Copeman⁴⁸ discovered Charcot-Leyden crystals in the blood of a leukæmic, both before and after death, but many more after death; Westphal⁴⁹ found the same crystals in fluid drawn from the spleen during life.

Von Jaksch⁵⁰ claims that peptone can be demonstrated in the blood where disintegration is marked, as in leukæmia.

Mathes, of Jena,⁵¹ examined the blood of 2 cases of leukæmia for peptone and allied bodies. In neither did he find peptone, but in each deutero-albumoses were demonstrable in the blood and serum.

Xanthin and hypoxanthin are present in the blood, as well as lactic and formic acids, according to Strümpel.⁵²

Freund and Obermayer⁵³ found a notable decrease of fixed substances and a notable quantity of peptone in the blood of leukæmic individuals. Upon chemical analysis the spleen yields xanthin, hypoxanthin, glutin, glycocoll, leucin, and tyrosin. The same authority (Roberts⁵⁴) says there is an increase in the fat and fibrin in the blood, with albukalin, mucin, and acetic acid, together with xanthin, hypoxanthin, lactic and formic acids. Bohland and Schurz⁵⁵ have determined that the excretion of uric acid is increased in leukæmia. Toulmin⁵⁶ reports 2 cases of leukæmia in negroes, one being interesting on account of a malarial history and the disappearance of leukocytosis, with diminution in size of the spleen under treatment with arsenic. Quinke⁵⁷ and Stintzing both observed a recession of the symptoms of leukæmia after the onset of general miliary tuberculosis. Engelhardt of Riga⁵⁸ records a case in which there was an attack of hæmoglobinemia, hæmoglobinuria, and icterus.

The case of lymphatic leukæmia here reported came under the observation of Dr. Julius Salinger in the Jefferson Hospital in 1900, and to whom the writer is indebted for the clinical history of the case.

The clinical notes are: K. S., aged forty-eight years, female, white, married. Mother died of tuberculosis at the age of fifty-six; father died of apoplexy at fifty-four; one brother died of tuberculosis; three other brothers also deceased, causes unknown.

In childhood the patient had measles, mumps, scarlet fever, and two attacks of diphtheria; good recovery followed all these diseases. Menstruation was first noticed when twelve years of age. The periods were painless, the flow profuse, lasting from three to seven days. One child was born to her when she was thirty years of age, and she had no miscarriages. Six years ago she had peritonitis, the attack lasting two weeks, with eventual good recovery.

Six weeks before coming under observation the patient noticed dyspnœa on slight exertion. The attack of dyspnœa was followed by severe pain, more or less periodical. This pain (dull and gnawing) was limited to an area reaching from the lower margin of the last ribs to the anterior superior spine of the ilium on the left side. Relief was obtained by assuming the prone position and when

lying on the left side. Edema of the arms and legs followed these attacks of pain, which condition persisted for several days, leaving her in a very much weakened condition. Headache, vertigo, and impairment of vision (as of a scum over the eyes) were also prominent symptoms. Bowels were constipated, tongue coated, appetite fair.

An examination of the sputum was negative as regards tubercle bacilli. Examination of the urine resulted as follows: color, lemon yellow, clear; specific gravity, 1010; reaction, acid; albumin, a trace; sugar, none; urea, 1 per cent. Microscopic examination showed oxalate of lime crystals, amorphous urates, and a few squamous epithelial cells. No casts were demonstrable.

Repeated examinations were made of the blood, and these are appended:

June 19, 1900.	Hæmoglobin	25 per cent.
	Erythrocytes	1,000,000
	Leukocytes	22,500

No differential count made.

June 20, 1900.	Hæmoglobin	25 "
	Erythrocytes	931,200
	Leukocytes	23,000

Differential count of leukocytes was:

Small lymphocytes	62.5 "
Large lymphocytes	3 "
Polynuclears	32 "
Eosinophiles	2.5 "

July 7, 1900.	Hæmoglobin	25 "
	Erythrocytes	1,000,000
	Leukocytes	2,500

Differential count of leukocytes was:

Polynuclears	69 "
Small lymphocytes	23 "
Large lymphocytes	8 "
Eosinophiles	0 "

July 18, 1900.	Hæmoglobin	25 "
	Erythrocytes	1,240,000
	Leukocytes	2,800

Differential count of leukocytes was:

Polynuclears	70 "
Small lymphocytes	22 "
Large lymphocytes	8 "
Eosinophiles	0 "

Aug. 10, 1900.	Hæmoglobin	40 "
	Erythrocytes	1,204,000
	Leukocytes	4,000

Differential count of leukocytes was:

Polynuclears	63 "
Small lymphocytes	26 "
Large lymphocytes	10 "
Eosinophiles	1 "

Poikilocytosis was observed in this examination.

Aug. 16, 1900.	Hæmoglobin	35 "
	Erythrocytes	1,732,000
	Leukocytes	111,000

Differential count of leukocytes was:

Polynuclears	5 "
Small lymphocytes	90 "
Large lymphocytes	5 "
Eosinophiles	0 "

Aug. 22, 1900.	Hæmoglobin	40 per cent.
	Erythrocytes	1,672,000
	Leukocytes	85,009
	Differential count of leukocytes was:	
	Polynuclears	7 "
	Small lymphocytes	92 "
	Large lymphocytes	0 "
	Eosinophiles	1 "
	This count shows poikilocytosis and nucleated red cells.	
Aug. 28, 1900.	Hæmoglobin	85 "
	Erythrocytes	1,796,000
	Leukocytes	16,000
	Differential count of leukocytes was:	
	Polynuclears	20 "
	Small lymphocytes	79 "
	Large lymphocytes	0 "
	Eosinophiles	1 "

As a result of the blood examination a diagnosis of lymphatic leukæmia was made. The patient did not improve under treatment, but gradually grew worse, and died.

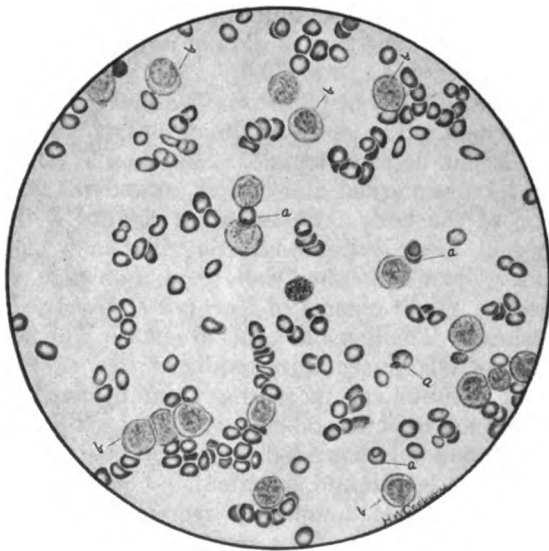
An autopsy was made, but permission was not granted to examine the nervous system. The notes of the autopsy follow: Body of a well-preserved, middle-aged female. Skin has a yellowish-brown or bronze tint, more marked and darker around the neck than any other portion of the body. Post-mortem rigidity well marked in both upper and lower extremities. Suggillation is slight in back and buttocks. Upon abdominal wall, scars, indicative of past pregnancy, are seen. Slight œdema of feet; few ecchymoses upon scalp near the forehead. The lips and gums are pale. The subcutaneous fat is well preserved; musculature reddish in color. Small epiplocele is present at umbilicus, measuring 3 cm. in diameter. Vessels of the omentum are injected; blood is still fluid. The larger vessels of the stomach are all distended and engorged. The appendix measures 10 cm. in length and is intimately bound down by mesentery. The liver extends completely over to the left side and to 5 cm. below the umbilicus. The peritoneum contains 100 c.c. of slightly cloudy fluid. The pericardium contains 100 c.c. of clear, straw-colored fluid; otherwise it is normal.

Right side of heart is dilated. The right auricle contains a large number of chicken-fat clots, together with a large quantity of fluid, watery blood. Right ventricle contains a few currant-jelly and chicken-fat clots and fluid blood; while the left auricle and left ventricle are comparatively empty. As the heart is cut from the great vessels a large number of small clots and a large quantity of blood wells out. Heart weighs 330 gms. Muscle is flabby, pale in areas, and there is an abundance of epicardial fat present. The right ventricular wall is thin, and the adipose tissue represents about two-thirds of its thickness. There is slight thickening of the tricuspid and mitral leaflets; aortic valve shows fenestration of middle leaflet; beginning atheroma of the aorta is also noticed.

Left pleura shows marked general adhesions; the lung is compressed and markedly œdematous. Weight 480 gms. Right pleura is universally adherent; the right lung is more œdematous than the left. Weight 570 gms. The spleen is large, dark red in color, measures 22 cm. by 17 cm. by 7 cm. The surface shows areas of capsulitis and the organ is adherent to the under surface of the liver. Upon section the organ cuts with slight resistance, and there is an apparent prominence of the Malpighian bodies; no amyloid reaction could be obtained. Weight 300 gms. The left adrenal shows no appreciable change macroscopically.

The left kidney is movable, enlarged, pale, and flabby, and measures 16 cm. by 3.5 cm. by 2.5 cm. and is slightly lobulated.

FIG. 1.



It cuts with some resistance. The organ is pale throughout; there is a slight increase of adipose tissue in the pelvis. The capsule strips with ease and the surface is smooth. Weight 180 gms.

The right adrenal is apparently normal.

The right kidney is also slightly movable, lobulated, flabby, and cuts with ease; the substance is pale. The capsule strips easily, leaving a smooth surface. Weight 170 gms. Both ureters are normal.

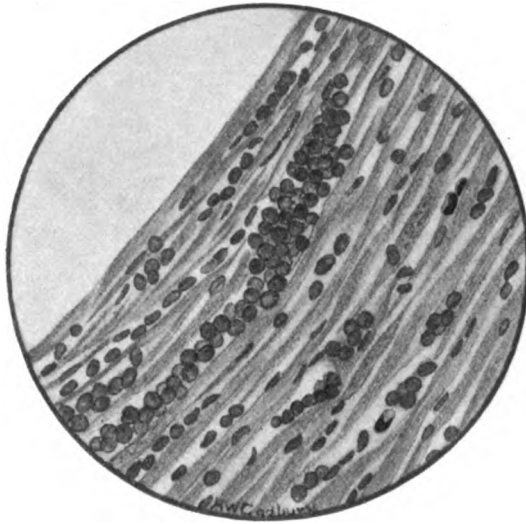
The liver, as mentioned previously, extends completely to the left side of the abdominal cavity. It measures 33 cm by 23 cm. by 9 cm. The organ is slightly paler in color than normal and cuts with slight resistance. Throughout the substance small, whitish or yellowish-white areas, more or less continuous with one another,

are seen, which do not give the amyloid reaction. The upper surface of the liver shows few areas of peritonitis. The gall-bladder is distended and contains 30 c.c. of a black, tenacious, tarry fluid. The bile-duct is patulous; no calculi in gall-bladder. Weight of liver 2800 gms.

Upon the under surface of this organ there is a large number of small masses, 1 to 5 cm. in diameter, which cut with slight resistance. Upon the cut surface (of these masses) small, pinkish-white, translucent areas 2 mm. in diameter are noticed, which do not give the amyloid reaction. These masses are apparently enlarged glands.

The uterus is normal; the left ovary is prolapsed and cystic; right ovary is atrophied. The bladder is empty and its walls are

FIG. 2.



very much thickened. The stomach is apparently normal and shows the usual congestion noticed post-mortem. The pancreas measures 18 cm. by 3 cm. by 1.5 cm., and is apparently normal. Weight 95 gms. The intestines present no apparent lesions macroscopically.

Histological Examination. The musculature of the heart is swollen and slightly granular. The striations in some fibres, as well as the nuclei, have disappeared. In some areas the muscle nuclei are normal, muscle fibres are wavy or spiral, and in still others fragmentation is present. The capillaries are filled with leukocytes, few of which are finely granular oxyphiles, but mostly lymphocytes. Irrespective of the capillaries, numerous lymphocytes are found between the muscular fibres, some in single, others in double column.

In one specimen a large accumulation of these cells is seen occupying the spaces of a fragmented fibre—*i. e.*, situated between the separated ends. In another specimen areas made up of a delicate, wavy, homogeneous tissue are seen, in which are entangled lymphocytes. These areas seem to have taken the place of heart muscle destroyed by fragmentation. Very few red blood corpuscles are demonstrable, either in the capillaries or between the fibres. Numerous mast-cells or mucinoblasts are also noticeable. Oil globules, both small and large, are seen in those specimens fixed with osmic acid. A large number of slightly oval and some spindle-shaped cells (these latter being finely granular and having no apparent nucleus) are also demonstrable, especially around the capillaries.

FIG. 3.



In examining the spleen the first thing that impresses the observer is the appearance of unusual cellular density of the sections. Enormous numbers of erythrocytes are seen scattered throughout; most of these are perfectly normal, exhibiting no fragmentation whatever. The bloodvessels are engorged, principally with leukocytes; some of the vessels show rupture of the coats, even those within the trabeculæ, while others show infiltration or dissection of the coats by lymphocytes. The whole splenic pulp seems to be made up of two cells—erythrocytes and lymphocytes. The Malpighian bodies are not at all prominent, and in some the small artery is infiltrated with the cells. Upon closer examination small masses of lymphocytes are seen, more or less cylindrical in shape, which correspond to leukæmic infarcts. Few mast-cells are demonstrable.

The capsule of the organ is thickened and, to some extent, infiltrated with lymphocytes, even to the extreme periphery. Despite the presence of such a large number of erythrocytes in the splenic pulp there is very little pigmentation present.

The cells of the adrenals are slightly cloudy or granular. The cortical portion of the organs are infiltrated with lymphocytes. This is most marked in the zona reticularis; the zona fasciculata shows some, while the zona glomerulosa shows the least infiltration. In the medullary portion there is no appreciable alteration. The small quantity of adipose tissue surrounding the adrenal is also infiltrated with lymphocytes.

The left and right kidney show cloudy swelling, the nuclei of some of the cells being distinctly visible, others showing an entire

FIG. 4.



absence of nuclei. The protoplasm is distinctly granular; in some tubules only granular debris is present. Large areas of cellular infiltration are noticeable between the tubules, and to some extent obliterating them. At first glance one might think it was an area of acute infection, but upon closer examination the cells are found to be for the most part lymphocytes. Together with these is a large number of slightly granular, spindle-shaped cells which resemble those found in the heart. Besides the large areas of cellular infiltration mentioned above, single and double columns of lymphocytes are seen between the collecting tubules. The capsule of Bowman is also infiltrated with lymphocytes.

The liver shows an extensive and marked cloudy swelling of the parenchyma, the nuclei being for the most part entirely obscured

or very faintly outlined. Between the columns of cells throughout the entire organ are lymphocytes which encroach to such a marked degree upon the liver substance that a certain amount is destroyed. Small and large aggregations of lymphocytes are seen (irrespective of those between the cells), some circular in outline and others irregular, which correspond to leukæmic infarcts. These are visible to the naked eye. There is a slight degree of fatty infiltration present, but no evidence of a cirrhotic process. Under a higher magnification the liver substance appears more or less in islands, and together with the lymphocytes mentioned quite a few red blood cells are seen between the rows of liver cells. Histologically the pancreas is comparatively normal, showing only a few lymphocytes around the bloodvessels.

FIG. 5.



Examination of the intestine shows marked lymphocytic infiltration between the crypts of Lieberkühn and in the villi. There is no evidence of ulceration, but the enormous number of lymphocytes resembles very closely areas of infection. In the submucous and muscular coats large numbers of mast-cells are demonstrable, especially in the former. There are also a few of these cells seen in the villi. The bloodvessels are dilated and filled with lymphocytes.

The peribronchial and mesenteric glands show such an increased density that the typical arrangement is destroyed. There is also a certain amount of pigmentation present in the former. Few mast-cells are demonstrable.

There is no apparent increase in the elastica in any of the organs examined.

The bone-marrow of the ribs is extremely pale and scant. The cancellated structure is distinctly dry. Spreads made from the marrow contain lymphocytes and a few red blood cells, the latter mostly in islands. An occasional myelocyte and hyaline cell are seen. A few nucleated red cells are demonstrable, some exhibiting extrusion of the nucleus.

Spreads made from the heart's blood, spleen, and liver show exactly the same cellular elements as those from the bone-marrow.

Some granules of the polynuclear leukocytes and lymphocytes give the iodophilic reaction.

FIG. 6.



Inoculations were made from the bone-marrow, liver, spleen, kidney, and blood upon agar, blood serum, blood-smear agar, and acid agar. From the bone-marrow and blood a bacillus which resembled the bacillus coli communis, morphologically, tinctorially, and biologically, was obtained. From the liver no growth was demonstrable at the end of twenty-one days. From the spleen a diplococcus (which corresponded morphologically and tinctorially to the diplococcus of Sternberg) and the staphylococcus pyogenes aureus were isolated. From the kidney the bacillus pyocyaneus and staphylococcus pyogenes aureus were obtained.

The case is interesting on account of its rarity and the comparatively short duration of the illness. All the organs examined except the pancreas show the lymphocytic infiltration to a marked degree. The infiltration of the peribronchial glands and conse-

quent enlargement would, no doubt, account for the dyspnœa. The bacterial findings apparently indicate an agonal infection.

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SPECIMEN FROM A CASE OF RHINOPHYMA.

BY A. G. ELLIS, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

The patient from whom this specimen was removed was a tailor by occupation. There was no history of trauma of the nose. Fifteen years ago he had an attack of what was probably acne rosacea, in which the nose and adjacent borders of the cheek were most prominently involved. This was followed by a nodular growth of the nose, involving all except the upper fourth of that organ. The growth was bluish-red in color, gave rise to no pain, and breathing was not interfered with; the projecting mass of tissue, however, caused serious annoyance to the patient while eating, and for this he sought relief.

Operation consisted in removal of the central portion of the growth by means of an elliptic incision and paring down of the part on each side that could not be thus included. Contrary to expectation, there was but little hemorrhage. The wound healed by first intention. The cosmetic result, as shown by the illustrations, is very satisfactory, quite normal-appearing skin having been reproduced over the areas that were reduced by paring.

The specimen received for examination consisted of several masses of tissue, the largest being 4 by 5 cm. in extent and 1.5 cm. thick. One surface was formed of wrinkled skin bearing numerous small, nodular elevations. The color was darker than that of normal skin, being of a slightly bluish tint; scattered over the surface were many small, depressed, reddish areas that resembled punctate hemorrhages.

The histology of sections from this tissue is very simple. They are composed largely of fibrous tissue which, on one border, is

FIG. 2.

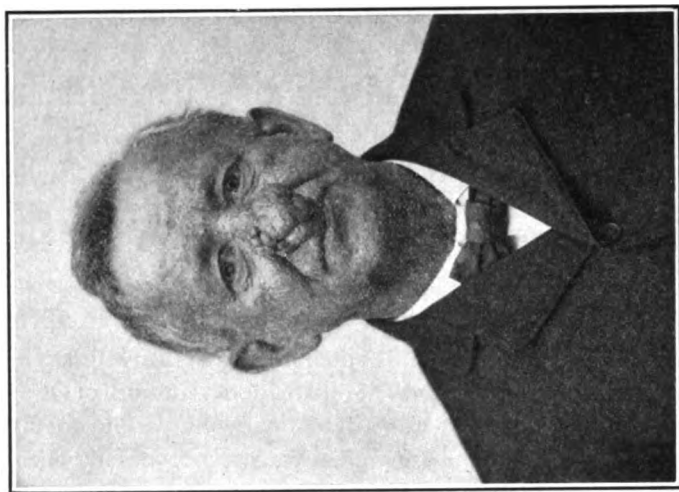


FIG. 1.



Rhinophyma. Appearance of patient before operation.

FIG. 4.

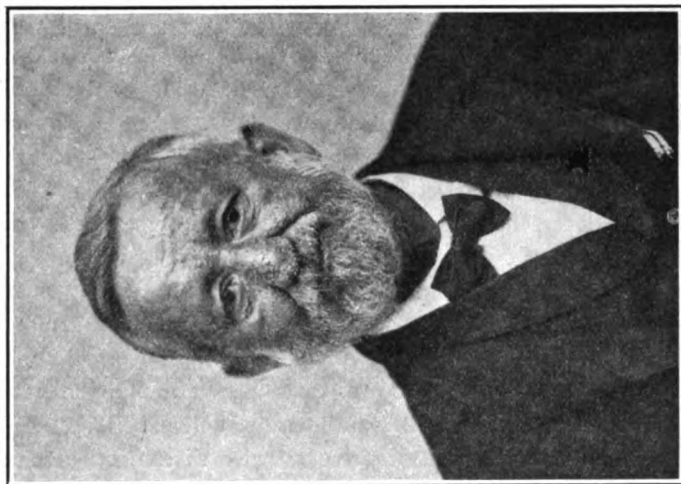
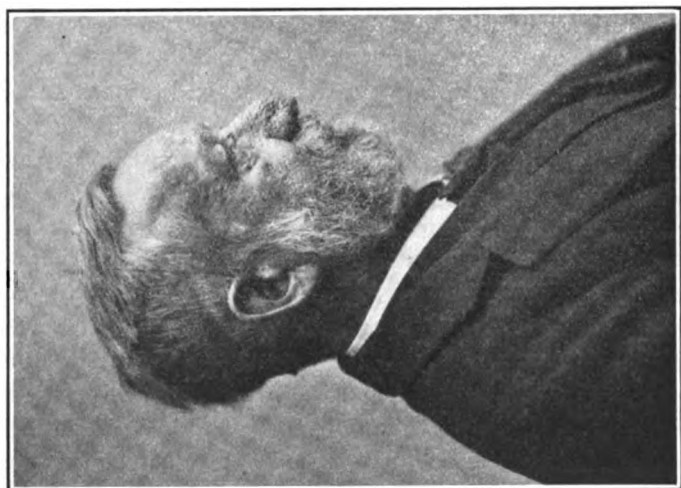


FIG. 3.



Rhinophyma. Appearance of patient after operation. The corrugated condition of the skin is more marked than on the nose itself.

marginated by stratified epithelium, such as is found in normal skin, though the layers are fewer in number than usual. The corium and subcutaneous tissue are directly continuous with and similar in structure to the deeper portions of the section, which are composed of a fairly loose, cellular fibrous tissue containing numerous lymph spaces and bloodvessels. The fibrils of this tissue are exceedingly wavy and irregularly placed. A very conspicuous feature of the sections is the sebaceous glands, which are greatly increased in size and in some areas apparently in number. Slight evidence of cystic change is shown by some of these glands, and in one instance the gland structure has almost entirely disappeared, the space being occupied by polynuclear leukocytes; there is, however, little or no evidence of inflammatory change in the surrounding tissue. Around certain of the hair follicles are quite dense accumulations of small mononuclear cells. The diagnosis given is soft fibroma of the skin with distention of the acini and possibly hyperplasia of the sebaceous glands.

The only recent reference to rhinophyma, an indefinite name that has been given to this condition of the nose, appears to be that of von Bruns,¹ who reports eleven cases, eight of which he operated upon. The condition is also spoken of as hypertrophy or elephantiasis of the nose; some writers consider it simply a late stage of acne rosacea, or a type of that disease they designate acne hypertrophica. Von Bruns believes acne rosacea and rhinophyma possess nothing in common; neither does he consider alcohol an etiologic factor in rhinophyma, which he attributes to the growth of congenital "anlage." The growth in his cases had persisted for from five to twenty years, the age of the patients ranging from fifty to sixty years. The apex and alæ of the nose are irregularly thickened; at times the affected portion is covered by lobulated projections that are usually sessile, but occasionally pedunculated. Deep grooves are sometimes present, dividing the growth into several, most often three, distinct lobes. In extreme cases the lobules hang over the upper lip and even upon the chin.

Von Bruns describes the growth as being soft in consistency and possessing a glistening, fatty surface, from which can be expressed plugs of ribbon-like masses of sebaceous; the color usually is purplish or bluish-red, sometimes gray, occasionally unchanged.

Histologically the growth is composed of vascular connective tissue and enlarged and cystic sebaceous glands filled with sebaceous material and epithelial detritus. Proliferation of epithelium is not present. The growth has been designated fibroma or cyst-adenofibroma, according as the fibrous tissue or cysts predominate. This essentially describes the present specimen except that cystic change is here almost entirely lacking.

The privilege of studying and presenting this specimen, the notes of the case, and the accompanying illustrations, I owe to Dr. W. W. Keen,² who has elsewhere reported the case in full.

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TRYPANOSOMA DISEASES.

BY W. M. L. COPLIN, M.D.,

AND

A. G. ELLIS, M.D.

Dr. Coplin and Dr. Ellis presented a communication on trypanosoma diseases. They briefly described the known forms of the parasite and exhibited specimens of the *Trypanosoma lewisi* in the blood and tissues of rats. Through the kindness of Dr. Kin-youn they were able to show the *Trypanosoma brucei* in the blood of a horse. They had inoculated a large number of white rats with blood containing the *Trypanosoma lewisi* obtained from Dr. Novy, of Ann Arbor. In three inoculated white rats the parasites could not be demonstrated in the blood after the forty-fifth day, and in one after the fifty-ninth day; in one gray rat (Blockley) the parasite was still present in the blood seventy days after coming under observation. Although several of the rats died, in none of them was there reason to believe that death had resulted from trypanosoma infection, with the possible exception of one in which, at autopsy, a beginning pneumonia of a catarrhal type was found. No cultures were made from this case, but bacteria could not be found in the sections. This was of interest, as in one of the cases of reported human trypanosomiasis the patient had developed a pneumonia, from which, however, she recovered.

Control rats kept with the infected animals did not acquire the parasite. The urine from a dead inoculated white rat contained no trypanosomas, although the blood was full of them. Usually the parasites disappear from the blood postmortem, but in one case they were demonstrable thirty hours after death.

For the purpose of determining the frequency of infection, Dr. Coplin and Dr. Ellis had examined forty-three rats from the Philadelphia

Hospital, and found twenty-five (58 per cent.) infected. Of seventeen rats caught in the Jefferson Medical College, nine (53 per cent.) contained parasites. Dr. Glenn, of Asheville, North Carolina, was kind enough to send sixteen barn rats; five (31 per cent.) of these were infected. Of 6 barn rats examined near Clarksburg, West Virginia, none were found to contain the parasite. The infection is much more common in young rats. In the Philadelphia Hospital series no full-grown rat was found infected. Of the rats caught at Jefferson, two evidently old animals contained the parasites. The authors have not found trypanosomas in the saliva of infected rats; and dead infected rats were frequently eaten by others, the latter not acquiring the infection. The parasites were not present in a number of fleas found on infected rats. A litter (six) of young rats born of an infected mother (inoculated white rat) contained no parasites. One of the observers has been bitten twice by infected rats without any untoward results. Five mice and a bat were examined, but no trypanosoma was found.

A CASE OF MULTIPLE CEREBROSPINAL SCLEROSIS.

WITH REMARKS UPON THE PATHOGENESIS OF THE AFFECTION.

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(From the Jefferson Medical College Laboratories.)

THE consensus of opinion regarding the frequency of multiple sclerosis is that it is a rare affection in this country. This view is based upon the fact that typical cases presenting the classical symptoms are comparatively few. We should not, however, forget that in its early stages and in certain cases even in the latest stages the diagnosis of the affection is exceedingly difficult; perhaps, therefore, the disease is less frequently recognized than we would expect. Charcot had long ago pointed out the polymorphous character of this curious disease and the erroneous diagnosis made in many cases. Recently Hoffmann (*Deutsche Zeitschr. f. Nerv.*, 1902) has expressed the same view. Indeed, he maintains that the affection is one of the most common of organic nervous diseases. Being clinically often difficult of recognition, the thought arises whether the low percentage of cases in this country, as compared with Europe, may not in part be due to the small number of necropsies reported. In fact, as far as we know, only six cases with pathological findings have been reported in the United States: two by Spiller, two by Spiller and Camp, one by Burr and McCarthy, and one by Hunt. The following case is, therefore, the seventh:

L. C., female, aged twenty-nine years, white, entered the Philadelphia Hospital August 26, 1903, with the following history: Complaining of pain and tenderness in the pelvic region and profuse leucorrhœa. She was admitted to the gynecological wards. She had menstruated at twelve and had married at seventeen. She had never had living children, but three miscarriages. Three years previous to admission she fell and struck on the buttocks; since then the nervous disturbances enumerated below gradually developed. An operation showed cystic ovaries of long standing. Oöphorectomy was performed. Later she was transferred to the Nervous Wards, where the following symptoms were elicited. The body was much emaciated and distinct atrophy of individual groups of

muscles, especially those of the thenar and hypothenar, were noted. There was complete loss of power in the lower extremities. She could not flex or extend her legs. There was double foot-drop; the left foot was rotated inward. The knee-jerk was increased on both sides; ankle clonus existed on the right; Babinski was present on both sides. Examination for sensation showed a hyperalgesia of the whole body. The patient complained also of considerable pain in the joints, especially in those of the shoulders and hips.

There was a very coarse intention tremor, more marked on the right than on the left. The speech was distinctly scanning. Lateral nystagmus was present in both eyes. The pupils were unequal, the right larger than the left; they responded to accommodation, but very little, if any, to light. The left eye showed slight ptosis. Ophthalmoscopically the eyes were not examined. There was incontinence of feces and urine. A large bed-sore was present over the sacrum. Gradually the knee-jerks began to disappear; at first on one side, and then on the other. When shortly before death she developed a profuse diarrhoea, the knee-jerks were entirely gone. She died October 2, 1903.

The autopsy showed hypostatic congestion of the lungs, chronic parenchymatous nephritis, pyelonephritis, cystitis, and colitis. The brain was deeply injected; the pia-arachnoid slightly oedematous. Beneath the tentorium there was a large amount of clear, straw-colored fluid. The dura of the spinal cord was distended likewise with a straw-colored fluid.

MICROSCOPIC EXAMINATION OF THE BRAIN, CORD AND PERIPHERAL NERVES.

Cord. Cervical Portion (Weigert and Weigert-Pal methods). Transverse sections reveal great areas of sclerosis involving extensive destruction of the nervous tissue. From above downward the anterior cornua have gradually disappeared. In the upper levels the most anterior portions only are preserved, while in the lower cervical segments they are entirely absent. In the white substance the sclerotic areas also have entailed extensive destruction and some degeneration of fibres. In the upper segments the anterior white columns are intact, but as we descend to the thoracic portion they become gradually reduced. The lateral columns and the posterior columns of the cord, on the contrary, are almost entirely absent in the upper levels, but are preserved to some extent in the lower levels. A small band of healthy fibres is seen at the periphery of the cord surrounding the sclerotic areas. It is to be noted that healthy fibres are everywhere intermingled with the degenerated ones. The degeneration as well as the sclerotic areas are not symmetrical nor equal in extent in the two halves of the cord. The posterior roots show distinct degeneration at the level of their entrance into the cord, but only on one side. The anterior roots

also show some degeneration in the lower cervical portion. The bloodvessels around the cord show distinct dilation with thrombotic foci, and in some places present signs of endoarteritis and periarteritis. Marchi's method shows clearly very marked recent degeneration in areas which are apparently normal with Weigert's stain.

Thoracic Region. As in the cervical cord, there is extensive discoloration of the gray matter. In a small portion only of the thoracic cord are parts of the anterior cornua preserved; all the rest of the gray matter is destroyed. The anterior white columns, as in the cervical cord, are intact. The reduction of the anterolateral columns continues down the dorsal cord, so that we find only a very small area preserved on one side and extensive degeneration on the other. The posterolateral columns are totally destroyed with the exception of a few fibres in the direct cerebellar tract on one side and an extremely narrow peripheral band on the other. The posterior columns are entirely destroyed on one side, while on the other they are reduced to a few fibres. The posterior roots are destroyed on one side and much degenerated on the other. The bloodvessels are in the same condition as in the cervical region. Marchi's method shows recent degeneration in the pyramidal tract and in the posterior columns.

Lumbar Cord. There is complete destruction of the anterior portion of the anterior cornua. The anterior white columns and anterolateral ground bundle are destroyed in the upper portion, but only partly degenerated in the lower portion. The crossed pyramidal tracts show distinct degeneration through the entire lumbar segment. The posterior columns, as well as the roots, are normal. The bloodvessels are unusually dilated and thickened, especially in the lower portion. Marchi's method shows recent degeneration in the anterior columns only in the upper cervical segment.

The *sacral cord* shows almost complete absence of gray matter, and the white substance contains only degenerated fibres. The roots are intact. The bloodvessels show the same changes as in the other portions of the cord.

Medulla. In the lowest segment the nuclei of the columns of Goll and Burdach are totally destroyed; in the columns themselves there remain very few fibres; the rest are degenerated; the same condition is noted in the decussating fibres. At the level of the beginning sensory decussation there is seen the same destruction of the nuclei gracilis and cuneatus, areas of degeneration in the posterior columns, and a marked sclerotic area in the sensory decussation. In sections above we see reappearance of a great many fibres in Goll's and Burdach's columns, but intermingled with a great many degenerated fibres, more upon one side than upon the other. The above-mentioned nuclei, also Monakow's nucleus are entirely absent. The destruction of the sensory decussation extends forward, but unequally, into the pyramids, and involve also a large

part of the nucleus of the hypoglossus. Very few cells are seen in the nuclei of the eleventh and twelfth nerves. In upper sections we see the sclerotic process involving also the gelatinous substance of Rolando, the fasciculus solitarius, the nuclei of the eleventh and twelfth nerves, the interolivary portion of the formatio reticularis alba and portions of the pyramids. These changes are not symmetrical.

In sections above, the nuclei of Goll and Burdach reappear again, but unequally, on both sides; the sclerotic process is seen to extend to the restiform bodies. Gradually in sections higher up the

FIG. 1.

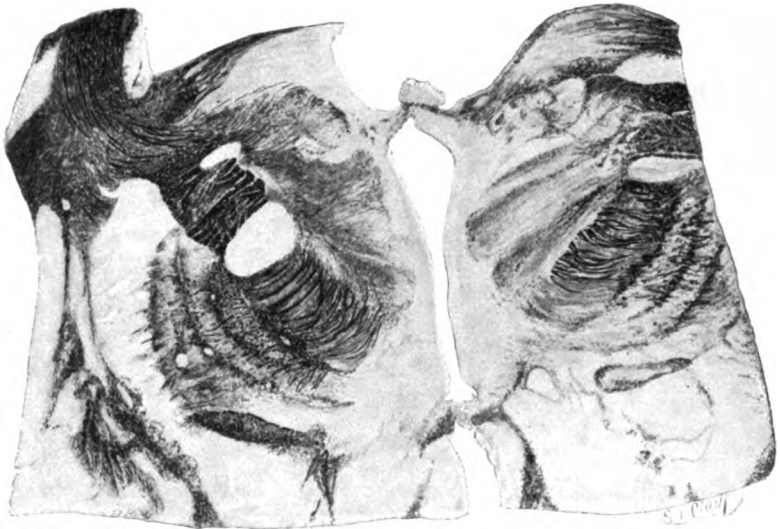


Besides other sclerotic areas, degeneration of the optic tracts and partly of their chiasma are to be noted. Also the crura are involved.

nuclei and the columns of Goll and Burdach become more and more free from the sclerotic process and show only degeneration. The latter process involves also the cerebello-olivary fibres which surround the descending root of the fifth nerve. The pyramids also show only degenerated areas. In the sections following, the nuclei of the eighth, ninth, and tenth nerves also reveal partial destruction. Higher up we see also that the tuberculous acusticus, the two nuclei of the eighth, the solitary bundle, the olives with their afferent and efferent fibres, are more or less and unequally on either side involved; the pyramids always show areas of degeneration. The posterior longitudinal bundle, the median fillet, the trapezoid body, and the

inferior cerebellar peduncles are also partly destroyed. Similar conditions are noted in the knee of the seventh, in the nucleus of the sixth, in the descending sensory root of the fifth; also in the posterior transverse fibres of the pons and in the pyramidal bundles. At the level of the cerebellum we see that the three cerebellar peduncles, both roots of the fifth nerve, the middle lobe of the cerebellum, besides the pyramidal bundle—all suffer considerably. At the level of the aqueduct of Sylvius, the pathetic nerve is almost entirely destroyed on one side. In the subthalamic region one red nucleus and one posterior longitudinal bundle are more or less degenerated. The optic tract in front of the mammillary tubercles is totally degenerated on one side and slightly on the other. The

FIG. 2.



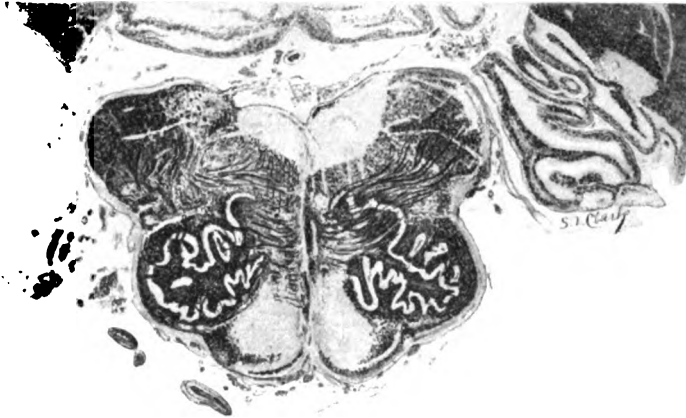
Plaques of sclerosis, particularly in internal capsule and crura.

foot of one cerebral peduncle is markedly degenerated in its inner third and the other in its middle third. A vertical section through the posterior limb of the internal capsule, at the level of the posterior commissure and the pineal body, shows an area of degeneration in the middle of the internal capsule; the degeneration involves also the fibres passing from the optic thalamus to the capsule and the posterior commissure itself. The degeneration is also seen to involve the fibres going from the thalamus to the cortex. Areas of degeneration are found besides in the white matter of the motor area of the brain and in the cerebellum. The bloodvessels of the medulla show the same change as in the cord.

A review of the pathological findings show that the condition of the gray matter is as follows: In the sacral portion of the cord

it is totally absent, in the lumbar cord it is preserved, and again begins to disappear in the thoracic and cervical segments. As to the white substance, it is preserved to a great extent in the lower cord, but in the thoracic segments, while it presents areas of degeneration, it contains also vast areas of total destruction, irregularly distributed. The height of the destruction is reached in the cervical cord. In taking up the individual tracts of the cord, we see that the anterior and the anterolateral columns are gradually reduced from above downward. No such regularity could be traced in the posterior and posterolateral columns. The irregularity of the sclerotic process is particularly marked in the medulla; while in one section the areas of destruction are multiple and extensive, in others there is merely a marked diminution. However, we can say that the gray matter—viz., the nuclei—suffers more than the

FIG. 3.



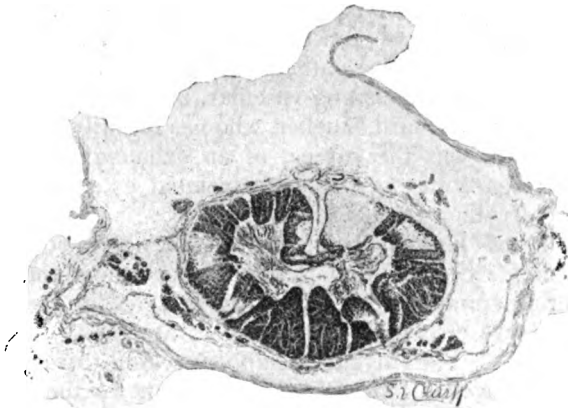
Sclerotic areas in the pyramids and restiform bodies.

fibres. Almost all of the nuclei of the cranial nerves and the nuclei of the medulla and pons are affected. The motor as well as the sensory decussation, various afferent and efferent fibres of the olives, the three pairs of cerebellar peduncles, the pyramidal bundles, the middle lobe of the cerebellum and the hemispheres of the latter, the geniculate bodies, the red nuclei, the posterior longitudinal bundles, the internal capsule, the thalamic fibres going to the internal capsules and to the cortex, finally the optic tracts—these are the structures affected by this curious disease process. The characteristic feature consists in the remarkable irregularity of the distribution; the site and extent of the pathological areas vary from section to section, and there is no symmetrical arrangement of the patches in the two halves of the sections. Marchi's method always showed recent degenerations among the preserved fibres. The

bloodvessels showed, all along the cerebrospinal axis, distinct and in some places marked dilatation and thickening of their walls. Leukocytic infiltration of the walls of the bloodvessels and thickening of the meninges with nuclear infiltration are seen at the periphery and in the fissures of the cord.

The condition of the cells and of the axis cylinders deserve special mention. In contrast with the extensive foci of sclerosis in which the fibres of the white matter are entirely destroyed, we found, curiously enough, marked preservation of a large number of cells; even in the midst of an entirely discolored portion, showing total destruction of tissue. Thionin stain revealed some cells intact. It is true that in similar areas the majority of cells are absent, but it is certainly surprising to find normal cells in foci of such a character. A quite considerable number of normal cells are seen in

FIG. 4.



Anterior and lateral columns show areas of sclerosis. Secondary degeneration.

areas where the nervous tissue, if not entirely, is at least to a great extent damaged. A glance at these findings gives the impression that the destructive process had originally no predilection for the cells, which it, as it were, avoided and affected only the white substance. There are, however, some degenerated cells in which are to be seen the usual chromotolysis, with displacement of the nuclei and deformities of the entire cell.

Similar remarks can be made about the axis cylinder. Not only among the ordinary degenerated fibres, but also in the completely destroyed areas, axis cylinders are seen to be present. Naked axis cylinders are found scattered in the most diseased areas. Transverse sections, however, show that they are irregular in form, angular, large, or unusually small (atrophy). That they are diseased there cannot be any doubt, but the fact that they are present, without their medullary sheaths, even in dense islets and sometimes

normal in shape and size, is strongly suggestive of the view that the sclerotic process has a tendency to affect primarily the medullary sheaths and spare for a long time the axis cylinders.

The pathogenesis of disseminated sclerosis is still a subject of discussion. According to the vascular theory, the destruction of nerve tissue is secondary to a primary alteration of the vessel walls. Although in a number of cases endarteritis and periarteritis have been found in multiple sclerosis, some competent investigators have failed to find such lesions, or, at least, changes that are characteristic and pronounced. Our case presents dilatation and thickening with leukocytic infiltration of the vessel walls, but these changes are not equally nor extensively distributed. Moreover, in certain regions, in which the destruction of nerve tissue is the least marked, the vessel changes are the most pronounced, as, for example, in the lumbar segments of the cord. In other words, the degenerated condition of the vessels is not in keeping with the destructive process in the nerve tissue. It is very probable that these changes do not bear to each other the relation of cause and effect. Further, it is not impossible that the same pathogenic agent (whatever it may be) affects both tissues, nervous and vascular, at the same time, though in varying degree. Eduard Mueller, who has recently made multiple cerebrospinal sclerosis the subject of an exhaustive treatise, goes so far as to regard the vascular involvement as secondary to the involvement of other tissues.

Regarding the lesions themselves, it is noteworthy that the nervous elements proper—that is, the axis cylinders and the nerve cells—suffer last and least. All observers agree in the frequency with which nerve cells and axis cylinders are found intact in the sclerosed areas. The myelin disappears long before the axis cylinder is destroyed. This doubtless accounts for the infrequency and merely occasional presence of secondary degeneration. Whatever the origin of the disease really is, it is not impossible that we have to deal here with a sclerosis of the neuroglial tissue. This position is strongly advocated by Mueller. In confirmation of this view, Mueller points to an instance observed by him in which multiple sclerosis and syringomyelia coexisted in the same patient. He would, indeed, regard multiple cerebrospinal sclerosis as a multiple gliosis of the nervous system. However, the rarity of the concurrence of syringomyelia and multiple sclerosis would alone throw doubt upon this interpretation. Furthermore, gliomatous lesions of the nervous system observed elsewhere than in the cord are not in any sense comparable to typical plaques of sclerosis. Again, there are many facts which render a theory that this disease is dependent upon some abnormality of tissue development, embryonal or otherwise, untenable. That the lesion may have its origin in the glia is not impossible. However, all that we have a right to infer is that neither the nerve cells nor axis cylinders,

on the one hand, nor the bloodvessels, on the other, are primarily involved.

An interesting pathological feature of our case is found in the presence of secondary degeneration, which, as is well known, is a rare occurrence in multiple sclerosis. Beginning in the motor area and continuing through the internal capsule down to the medulla and the very lowest portion of the cord, we found in the pyramidal tract, besides isolated sclerotic islets, also degenerated fibres intermingled with normal ones. We are, however, unable to say whether this secondary degeneration is an independent condition or is in relation with the sclerotic foci.

Finally, we wish to call attention to an interesting phenomenon observed during the patient's life, and which was of some diagnostic importance—viz., the condition of the knee-jerks. While at first they were exaggerated and remained as such for a long time, they gradually diminished in intensity and finally disappeared. This was an indication of an extension of the pathological process from the white matter to the gray. We consider this observation noteworthy, as some competent authors (Marie and others) believe that the knee-jerks are never absent in disseminated sclerosis. As a last interesting feature of the case we wish to emphasize the involvement of the third, fourth, and sixth nerves, with their nuclei, and also the optic tracts.

PRIMARY TUBERCULOSIS OF THE FEMALE BREAST, WITH A REPORT OF A RECENT CASE.

BY

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M. K., aged 20, single; birthplace, Ireland; occupation,
housework; was admitted to the Jefferson Hospital, July 25,
1904.

The patient's father, three sisters and one brother are living
and in good health; her mother died in confinement. There is
positively no history of tuberculous disease in the family.
When a child, she had measles and pertussis. With these
exceptions, she has always had perfect health until the present
trouble, which began about a year and a half ago. There is no
history of traumatism. One year ago she was operated upon
for enlarged glands of the right axilla, some of which had
broken down and were discharging pus. She asserts that at
this time there was a tumor in the outer side of the same breast,
which was not removed. This tumor was observed some time
before enlargement of the axillary glands, and since the operation
on the glands, pressure on the tumor expels fluid from the
lower part of the axillary incision.

When admitted to the hospital, physical examination showed
the patient to be unusually well nourished, robust, and appar-
ently in the best of health. Examination of the heart, lungs, spu-
tum and urine revealed nothing abnormal. In the upper and
outer quadrant of the right breast was a distinct mass about
three fingers in width and four in length, nodular, hard below,
and cystic above, and quite movable. At points, the skin
seemed to be adherent. In the axilla was a scar, which marked
the site of the former operation. There was a sinus at the lower
end of the incision. Just above the upper limit and a little in-
ternal to the breast, was another sinus. On pressure over the
mass in the breast, a fluid resembling pus flowed from both
sinuses. This breast was larger than the other, but never was
the seat of much pain. The other breast and axilla appeared
normal in every respect.

On July 27, 1904, two days after admission, I operated. On
account of the sinus, which was above and internal to the
breast, it was impossible to make the Halsted incision. I cir-
cumscribed the breast by two curvilinear incisions in such a
manner that the apex of the incision pointed toward the junc-
tion of the inner and middle thirds of the clavicle. I then pro-
longed the apex of the incision outward and terminated it just
above the anterior axillary fold. This incision gave me access
to the enlarged glands of the axilla, and also to both sinuses.
The entire breast was amputated, together with the axillary
glands, fat, and fascia. The mass was sent to Professor Coplin
for a pathologic and microscopic examination. He made the
following report:

Specimen.—Tissue from right breast and axilla.

Specimen consists of an elliptic mass of tissue 14 cm. long,
6.5 cm. wide, and 4.5 cm. thick; weight, 281 gm. Two surfaces
are presented for consideration. One consists of an elliptic
piece of skin 9 cm. in length and 5 cm. maximum width, and an
enclosing border of what appears to be adipose tissue. About

3 cm. from one end of the area of skin is the nipple, almost free from pigmentation and retracted to such an extent as to form a dimple. The other surface is an irregularly cut plane, composed of fascia, adipose and connective tissues. Lying between these two surfaces is breast tissue, normal in consistency and appearance, except in one small area a little to one side of the retracted nipple. Here a small cavity is found, surrounded by a wall of hard, firm tissue. This cavity had been incised and drained when the specimen was received.

Blocks of tissue were taken from the evidently diseased area, fixed, mounted, cut, and stained, according to approved laboratory methods.

Microscopically the sections consist of connective tissue in which are varying numbers of lymphoid cells; in some areas the cellular elements are scanty, while in others they are more abundant. This cellular connective tissue contains ducts and tuberculous glands lined with columnar epithelium; also a few bloodvessels whose walls are somewhat thickened. The interstitial connective tissue is notably increased, the gland lobules are infiltrated by lymphoid cells, and the fibrous walls of the duct are much thickened. In one end of the section a number of areas of greater pathologic significance are found. These areas are clearly marked out from the surrounding tissue, are circular in shape, and consist of a delicate connective-tissue matrix, supporting numerous leukocytes and epithelioid cells, while some of the areas also contain typical giant cells, and others give some evidence of beginning caseation. In a section stained with carbol fuchsin and decolorized by Gabbet's solution, typical tubercle bacilli are found.

A small irregular mass of tissue accompanied the specimen. It weighs 23 gm. and consists of four globular bodies, varying in diameter from 0.8 cm. to 1.7 cm., and bound together by fascia and adipose tissue. These little nodules are firm, tough, but not hard in consistency. Upon incision a thick, yellowish, creamy fluid escapes. Spreads of this fluid were made, and stained with carbol fuchsin, but tubercle bacilli were not found.

Pieces of the globular bodies were fixed and stained. Microscopically the sections consist of a fibrous connective-tissue capsule surrounding a mass of adenoid tissue. From this fibrous border, thick trabeculae extend toward the center, dividing the adenoid tissue into irregular pockets or compartments which vary considerably in density. In the center this fibrous framework entirely disappears, and the cellular elements are fragmentary and respond feebly to the stains. Along the border at one end of the section are small areas surrounded by a circular band of fibrous tissue, and composed of a delicate connective-tissue matrix supporting numerous lymphoid and epithelioid cells. Here and there in the fibrous border are bloodvessels with markedly thickened walls.

Diagnosis.—Tuberculosis of the breast with associated involvement of neighboring lymph-nodes.

In this case we were exceedingly fortunate in finding typical tubercle bacilli.

W. Scott Schley,¹ discussing primary tuberculosis of the breast, states that Gautier, in 77 collected cases of tuberculosis of the breast, found tubercle bacilli but 29 times. Scudder found the bacillus 29 times in 80 cases. Schley asserts other observers have failed to find the tubercle bacillus in over 100 resections. In view of these facts I feel justified in submitting to those interested in this subject, the report of my case as furnished me by Professor Coplin.

In speaking of its frequency, he states of all the neo-

plasmas of the breast reported, scarcely more than 100 have been reported as tuberculous. A number of these were doubtful and possibly examples of simple mastitis in tuberculous subjects. If we reject the cases not verified by histologic examination or the finding of tubercle bacilli, the number is reduced to about 65. Careful examination of these 65 cases shows that only about 12 can fairly be regarded as primary in the mammary gland itself, that is, if we exclude, as we must, all determinable foci of tuberculous disease elsewhere, involvement of axillary and supraclavicular glands, visceral infection, bone lesions, etc.

Admitting "no case is complete without an autopsy," nevertheless, judging from my patient's general condition, absence of tuberculosis in her family, failure to find evidence of tuberculous foci in other parts of her body, the secondary axillary involvement, the pathologic and microscopic examination, all prove if such a condition as primary tuberculosis of the female breast exists, my case should be recorded as such.

On carefully reviewing the literature we find there are five routes cited by which the breast can become infected by the tubercle bacilli: (1) Through the blood or lymphatic channels; most writers claim this as the source of infection; (2) through the milk ducts; (3) through a surface wound, such as an abrasion on the breast or a fissured nipple; (4) the breast may become involved through continuity of structure; (5) one case is reported in which the infection extended from diseased bone of the chest wall. A. E. Halstead and E. R. LeCount² believe infection in most cases is due to a retrogressive lymphatic tuberculosis from the axilla or from the thoracic cavity.

I cannot say how the infection took place in my case, but I think it probably gained entrance through an unnoticed abrasion on the breast or nipple.

Prof. Edward P. Davis reported a case of primary tuberculosis of the breast in the *Medical News*, in 1897, in which he seemed to think the breast became infected through contact with the mouth of a tuberculous individual. There is no doubt that functional activity of the breast and nipple strongly predispose to this disease. Powers³ states that of 35 recorded cases of tuberculosis of the breast, 1 was in a male, and 34 in females. Of the 34, 22 were married, and 21 of the 22 had borne children. Age is not of diagnostic value in this disease. It may occur in patients past the middle age of life, also in infants. In the majority of the cases reported, however, the patients were under 38, and comparatively few under 21. The youngest patient reported was a case of Demme's,⁴ the patient being under 1 year. The most advanced age recorded up to date is 53; an account of this case was given by Remy and Noel.⁵

There are only a few cases on record in which diagnosis was made prior to operation. In the majority of cases the diagnosis was not made until after the removed tissue was subjected to a microscopic examination. The diagnosis in my own case was made before operation and was based on the history, secondary axillary involvement, and by excluding such conditions of the female breast as simple cyst, chronic mastitis, fibroadenoma, sarcoma, carcinoma, and gumma. If I had seen the patient before the axillary involvement, in all probability I would have made a diagnosis of chronic mastitis or fibroadenoma. The best authorities claim that before the nodules soften and break, and in the absence of axillary involvement, the diagnosis cannot be made without a microscopic examination of the tissue.

Treatment.—Such operations as curetting and cauterizing sinuses, incising abscesses, removing the tumor without the breast, have not been attended by good results. I think radical operation is indicated, and in every case of unquestionable tuberculosis of the breast, the breast, together with the skin overlying the tuberculoma, the glands, fat, and fascia from the axilla should all be removed as one piece. This appears to be the safest way, to prevent recurrence and dissemination. Such was my procedure, and it has proved most satisfactory in every respect.

I am indebted to J. Howard Anderson, M.D., Resident Pathologist Jefferson Hospital, for the excellent report he made of this case.

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AN INTERESTING TUMOR AND ITS RELATIONS TO HEREDITY.*

BY

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This little tumor was a turnip-shaped mass, at one pole of which was attached a short and rather thick pedicle. By means of this pedicle it had been attached to the external surface of the little finger at the second joint. It gave the impression of a cyst, for, although resistant to the touch, this resistance resembled that of a vesicle filled with liquid. It measured 11 mm. to 12 mm. in its greater diameter and about 6 mm. in its lesser. The color was not pronounced to the naked eye, although it had been removed from a colored child. Following is the history of the case:

Mrs. M., colored, aged about 28, gave birth to a girl, who, though otherwise normal, had a turnip-shaped growth at the second joint of each little finger. Each was connected to the external surface of the finger by a short pedicle. These growths were allowed to remain for several days, and upon the fourth the obstetrician intended to remove them. Upon his visit, however, he found but one present, the other having apparently been pulled off during the night. Its stump was still bleeding, showing that the vascularity of the tumor was considerable, a point corroborated by histologic study of the other growth. The second was removed and given to me as of possible embryologic interest.

Investigation of the family history disclosed a rather interesting condition. The mother at birth possessed just two such growths upon the outer surface of each little finger at the second joint. This showed the symmetry of the inheritance. These were not removed early, as in the case of the baby, but were allowed to remain until she was 12. At that time they were removed by her mother, as they were considerably in the way and were a source of discomfort. The stumps bled profusely for some time and the outer two joints of each little finger seemed affected from that time on. At present these fingers are drawn up and in a crippled condition, and this condition is thought due to the removal of the little tumors.

Of still greater interest is the fact that Mrs. M's. mother at birth also possessed such tumors that seemed similar and were located upon the external surface of each little finger at the second joint. At the time, Mrs. M. remembered no more in

*I am indebted to Mr. E. N. Faught, of the senior class at Jefferson Medical College, for this interesting tumor and the family history.

regard to the history of her mother and since then the family has disappeared.

It seems that the growths upon the baby's fingers resembled those of the mother and grandmother. It can only be conjectured, however, that the microscopic pictures were the same, though this seems highly probable.

As no such case has come to my notice, it seemed of great interest, especially the incident of the transmission through several known generations and perhaps as many preceding generations. The symmetry of the condition and the fact that it occurred on the female side of the family are also points of interest. It seems to illustrate the adaptation of nature to peculiarities that may have cropped out accidentally and were then transmitted to the offspring for generations. It would be interesting to learn if any of the children of this last generation will possess such growths at birth. How far back among the ancestors this condition existed is not known, but it must have occurred quite a distance back, as it was reproduced with a symmetry and regularity and correctness that seems wonderful. Yet the cause, or causes, that lead to such growths in the first ancestor that showed them are unknown, and why such useless structures should be transmitted from generation to generation seems strange. Yet the transmission seems as perfect as the transmission of peculiar characteristics or traits.

Upon incision, the liquid contents, apparently lymph, escaped. Upon examining the growth it was seen to consist of an outer wall and an inner mass. The wall was comparatively thick and light-colored, giving no macroscopic evidence of having been removed from a colored child. The inner mass was dark red and resembled a thin walled cyst containing blood. This mass appeared to be attached to the wall at one point and was much smaller than the tumor itself. No attempt was made to open it.

The entire tumor was fixed in Heidenhain's solution, dehydrated in alcohols of ascending strengths, cleared in a mixture of equal parts of absolute alcohol and cedar oil, and then pure oil, infiltrated with paraffin and blocked. It was mounted so that the sections would be cut parallel to the long axis. The tissue cut readily and the sections were stained with hematoxylin and eosin, hematoxylin and van Gieson, hematoxylin and picric acid, safranin and picric acid, paracarmin and picric acid, Mallory's reticulum and Weigert's elastica stains.

Upon general examination, at a magnification of 55 to 96 diameters, the tumor was seen to consist of epidermis, derma and central connective tissue, the centrum. The epidermis surrounded the whole tumor and the entire mass resembled a cross section of a finger in which the bone was missing. For about two-fifths of the circumference of the growth the epidermis was detached and formed the wall; the remaining portion was firmly attached to the inner mass, except at one small area where a small cyst had formed. This no doubt would soon have coalesced with the larger cyst. The wall seemed

stretched, as further examination proved. The dark red color of the inner mass no doubt was due to the capillary reflex, as these vessels were exposed by the separation of the epidermis. As was seen later, these vessels were numerous and engorged with blood. Pigmentation was quite pronounced, though macroscopically none was suspected. In some areas the pigment was not limited to the epidermis, but was found scattered in the papillas of the derma. It did not extend beyond the bases of these papillas, however. The pigment was well shown in those sections stained with safranin and picric acid. The upper portion of the derma was papillated and contained many small bloodvessels and the ducts of sweat glands. The lower part of the corium contained the secretory parts of the glands, a great number of large bloodvessels and several pacinian bodies. The centrum seemed made up of a large number of darkly-staining fibers or bundles, resembling somewhat voluntary striated muscle. They were nearly all parallel, and in the upper sections studied, cross sections were few.

Under high magnification (265 to 750) the epidermis was seen to consist of four layers, stratum malpighii, stratum granulosum, stratum corneum, or perhaps lucidum, and a stratum pigmentum. In the separated portion of the epidermis, the wall of the cystic part, the layers were less characteristic. Over the small cyst the layers were no different than those of the united areas. This seems to indicate that this separation must have been recent, and that the pressure in the small cyst was not great, as all the papillary waves of the stratum malpighii were present.

Stratum Malpighii.—In the united area the basal or genetic layer of the stratum malpighii consisted of a single layer of very tall, slender columnar elements, each of which possessed a long and comparatively broad nucleus that averaged 6 microns by 10 microns. The cells above the genetic layer were irregular, and their boundaries indistinct. They were fairly large, nearly polyhedral, and the nuclei well separated from one another. These nuclei were nearly all uniform in size; usually circular in outline, and averaged 7 microns to 8 microns in diameter. Each was surrounded by a clear space that made the darkly-stained nucleus quite prominent. The cytoplasm responded well to the acid stains. In the separated part the papillary waves were not well marked. This was probably due to the fact that this part of the epidermis seemed to have been stretched to form the wall of the cystic portion. The nuclei here did not respond so well to the safranin, but the light area around each was more prominent.

This layer averaged 80 microns to 125 microns in thickness. The pigment was scattered along its lower border and was more abundant in the separated part of the epidermis, especially in that part at the junction with the united portion.

Stratum Granulosum.—In those sections stained with safranin the stratum granulosum was not apparent. The best results for this layer were obtained with hematoxylin and van Gieson. This stratum consisted of two or three layers of long, spindle-shaped cells. The middle of each cell averaged 9 microns to 12 microns, and contained a distinctly stained nucleus surrounded by a narrow, clear field. Each cell was about 50 microns long, and the protoplasm contained many small dark granules. The whole layer averaged 25 microns to 35 microns in thickness, and had a somewhat wavy course.

Stratum Lucidum, or Corneum.—This stratum resembled

the latter more than the former. It consisted of many layers of almost homogeneous material which gave a striated appearance. Nuclei were entirely wanting, although unequally stained areas appeared at irregular intervals. It averaged 75 microns to 125 microns in thickness and took a diffuse stain with safranin.

The Stratum Pigmentum.—This layer was peculiar in that it covered the external surface of the tumor. The amount of pigment was not great though it appeared so under the microscope. Macroscopically no deep color was apparent. The outlines of the individual cells could not be distinguished, though many layers were present. These cells were probably not over 5 microns in height as the separated layers did not exceed this in thickness. The pigment varied from coarse to fine granules, the latter being quite diffuse. The large granules varied from 5 microns to 8 microns and resembled nuclei, but they did not react to the basic stains. Where this stratum was thin the granules were usually large and closely aggregated so as to give a dark color. In the broader areas the pigment was finer and diffusely scattered. The protoplasm between the granules responded to the acid stains.

The pigment was not limited to the above layer as it was found in the strata corneum and malpighii in places. In these areas it varied from fine and diffuse to large and coarse. In several regions where the epidermis was separated from the corneum, pigment was seen in the latter. In one of these patches the granules were many, diffuse and small and extended to the bases of the papillae; in another the granules were fewer, closer, and closely arranged and limited to the apices of the papillae.

Dermis.—The stratum papillare resembled that of ordinary skin. The papillae were best shown where the epidermis was separated. They consisted of delicate white fibrous connective tissue surrounding large and prominent capillaries. These vascular papillae predominated over those that contained tactile corpuscles of Meissner. The endothelium of the capillaries showed so plainly, that the entire outline of these vessels could at times be traced. The vessels were all engorged with blood cells that were in good condition. A basement membrane beneath the stratum malpighii was not discernible.

The stratum reticulare contained many very large blood-vessels. The connective tissue was arranged in larger, coarser bundles than in the foregoing. A delicate reticulum was visible in places. In some areas large wavy bundles predominated; these usually continued into the centrum. The nuclei were usually numerous and distinct, varying in length from 20 microns to 50 microns; in other areas the bundles were denser and formed a close felt-work that contained but few nuclei.

In the lower part of this layer were seen the secretory portions of the sweat glands and the pacinian bodies. The sweat-glands seemed normal in structure and size. They formed a ring that enclosed the centrum and was visible to the unaided eye. The cells of the ducts were low cuboidal elements averaging 20 microns to 25 microns in height; each contained a large deeply-staining nucleus, which was usually about 10 microns in diameter. The diameter of the lumen about equaled the height of a cell, 25 microns. With van Gieson's stain the basement membrane of the secretory tubules could be seen. The muscle fibers that usually separate these cells from the membrane, could not be distinguished. The

endothelium of the capillaries that lay between the coils of the secretory tubule was very distinct.

The pacinian bodies were not numerous, numbering about six in a middle section. They were located more deeply than the sweat gland and were readily distinguished by their lamellar structure. The lamellas were well formed, and the nuclei of each distinct. The spaces between the various layers were prominent. Not many of these bodies exhibited a good section, but one showed an almost perfectly transverse cut. Near the middle of this one was seen the inner bulb, in the center of which was noted the distinct axis cylinder.

The *centrum*, on general examination, seemed to consist of many small, branching muscle fibers. When these were examined under the high power, however, no cross striations were visible, but each seemed to be made up of fibrils. The nuclei were not characteristic of voluntary muscles. To van Gieson's stain these bundles responded well, appearing as large, heavy bundles of fibers of white fibrous tissue. Nuclei, however, were unusually numerous; these varied from long, slender bodies 80 microns to 100 microns wide to shorter, heavier elements 20 microns to 30 microns long and 5 microns to 7 microns wide. Some of the bundles extended up into the derma, even to the papillary layer. Most of the fibers were in longitudinal sections, but cross sections were also seen. These latter increased in number as the lower pole of the growth was approached and the longitudinal sections correspondingly decreased. It seems as if these bundles all converged toward the pedicle in the lower part, and in the upper part of the tumor spread out like a fan.

Adipose tissue was not abundant, but was seen in patches in the lower part of the derma, but not in the *centrum*. It appeared normal.

Sections subjected to Mallory's reticulum stain showed that the most delicate fibrils were stained. When a magnification of 750 diameters was employed, the delicate fibrils of reticulum that supports the secretory tubules of the sweat glands were readily distinguished. The lamellas of the pacinian bodies responded to this stain also, and showed the concentric lamellation very well. Even the inner bulb exhibited a number of concentric blue lines, seeming to indicate that this part of the body consisted of concentric lamellas also. The wavy course of some of the smaller bundles was shown.

Sections stained with Weigert's elastica stain, indicated the presence of considerable elastic tissue. In the papillary portion of the derma this tissue was present in the form of delicate fibers that extended up into the papillas and formed the greater portion of these. In some papillas, the elastic tissue was not very abundant. In the neighborhood of the bloodvessels, however, it was more abundant, even though the vessels were small. In the lower portion of the derma the elastica was quite abundant in areas. In the lighter, looser regions, the elastica existed as delicate fibers that formed a loose network; in other regions the fibers were larger and coarser, ran a wavy course, and gave a dark appearance to the area. It existed in the sweat glands, lying between the coils of tubule. In the *centrum*, the heavy, thick fibers, or fiber bundles, responded to this stain. The cross sections that predominated in those sections nearer the lower pole of the tumor, were as distinct as the longitudinal sections that predominated higher up. It seems very strange, however, that these fibrils should react

well to both van Gieson's and Weigert's stains. Ordinarily, they do not exhibit the characters of the elastic fibers, except the wavy course, and yet they respond to the elastica stain.

The vessels of the tumor were unusually numerous, and very large for so small a growth. In the papillary layer of the derma, the capillaries were very numerous, large, and filled with blood cells in very good condition. In the lower part of the derma the largest trunks were found, and these were unusually large. They were all thin-walled, and some contained but few blood cells, while the others were filled. In the upper part of the tumor, these main trunks were not so large as those near the lower pole. They all seemed to converge toward the lower pole, from which extended the pedicle. Even upon careful examination with a $\frac{1}{2}$ oil immersion lens, no nucleated red cells were found, although the infant was but four days old.

Pigmentation is greater in these sections near the lower pole. It seems that the nearer the tumor to the skin the greater the amount of pigment. The amount in the stratum Malpighii is greater and it extends further and the same is true of the papillary layer of the corium. Here the amount of detached epidermis is also increased.

The pedicle was surrounded by the epidermis, which at no portion was separated. All the layers were distinct. The papillary layer of the derma contained no pigment. The elastic tissue was abundant and consisted of delicate fibrils. In the lower part of the derma, the elastica here and there consisted of large fibers, which had a longitudinal disposition. These occurred singly or in groups, but were not numerous.

The vessels of the pedicle were few but large. They possessed more distinct walls than higher up and had more muscular tissue in the medias. In the lower portion of the inner mass the vessels were numerous and large, and surrounded by the centrum. In the pedicle, vessels occupied the central part, replacing the centrum.

This tumor, from its position, seems to resemble a supernumerary finger. Its structure also is closely related to such a structure, but neither cartilage nor bone was found; instead a mass of peculiar connective tissue occupied the central area of the tumor, most of which responded to both the van Gieson and elastica stains. From the foregoing description the question naturally arises: Is this an aborted supernumerary digit?

On review of the literature on the subject, no cases were found in which the structure was given, though many interesting histories were noted. The following were chosen as of especial interest, representing supernumerary, deficient or suppressed and fused digits, bearing especially upon heredity.

Of supernumerary digits, the case cited by Dr. Hey^{1*}

* n.—Normal s. t.—Supernumerary toes s. f.—		fingers	great, great-grandfather				
			great-grandfather				
			grandfather				
			st.—n—n—n—n—n				
			st. st. st. st.				

shows a remarkable recurrence of the malformation in several generations. The condition first appeared in the great great-grandfather, in whom it was represented by supernumerary toes. It next appeared two generations further on in the grandfather's children. Of these children but one showed the malformation (supernumerary toes), and his one child possessed the same. Although none of the other children of the grandfather had a malformation, the children of three of the six exhibited in one instance supernumerary toes; the two others had two children each, and of those a supernumerary toe and finger occurred in each family.

A point that Dr. Hey failed to note in the *alternation* showed in the occurrence in the grandfather's children.

F. S. Sherwood² mentions in a whole family supernumerary digits on both hands and feet in two generations. These malformations occurred in both males and females. Under his own personal observation the condition was shown in the third generation.

One of the most interesting cases of suppression or deficiency is described by Heim.³ In this the malformation seemed to result from an acquired condition. The patient, aged 40, at about 19, injured the third finger with a needle. In two years, after considerable trouble, the finger and part of the metacarpal bones were removed. Her fourth child had malformed hands in which the digit was absent and the metacarpal bone was rudimentary and short.

Marshall⁴ mentions an interesting case. A child of seven months possessed fingers that ceased at the proximal phalanges and thumbs that were poorly developed. The same defect occurred in the toes, though not to the same extent. The mother was deformed in the same way. Of the mother's 11 brothers and sisters, *alternate* ones were affected in like manner. Her father had had the same malformation, beside double thumbs, and the condition alternated among his brothers and sisters. No information could be obtained as to the proportion of males and females affected. In the fourth generation of a collateral branch, the condition was represented in mother, son and grandson.

Armstrong⁵ cites cases of deficiency of phalanges and



A, natural size of the tumor. B, cross section after embedding: a, separated epidermis forming the smaller cyst; b, separated epidermis forming the larger cyst; c, central mass or centrum.

digits in several (3) generations. The children had one or more phalanges or digits missing and the condition was always symmetric, but the same in only two.

Under fused digits Dr. Hilbert⁴ cites a case in which the middle and index fingers of each hand and the middle and fourth toes of each foot were united in the soft parts. A common nail existed in all the deformities. Each foot possessed an extra hallux that articulated with the first metatarsal bone and lay parallel to the true hallux. The same is said to have occurred in father and grandfather. There are many other malformations on record, but these are of exceedingly great interest from a standpoint of inheritance. In all but one case they passed from generation to generation.

In the case of Dr. Hey we find the condition skipping three generations to appear in but one instance in the fourth, and in four of the fifth, alternating as the diagram shows. Marshall's case is interesting, because of the alternation. In the mother's family alternation occurred as it did in the father's. Both Armstrong's and Hilbert's cases represent three generations. The only one representing but one generation is of importance as it represents the transmission of an artificially produced condition to the child. It is the only one that gives any cause for the origin of the malformation, as none of the others have any such element.

CONCLUSIONS.

From its general structure the tumor represents a digit in which the bone is absent. Its position is suggestive of this, but its shape is against it. No description of any such tumor or description of the structure of the digits could be found. It exemplifies inheritance, and shows quite a persistence in extending through three generations. Its symmetry, location, and general appearance in the three generations bear this out. It was transmitted through the female side, and to the female only.

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ON HYPERNEPHROMA.*

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HISTORIES OF THE CASES AND SURGICAL TREATMENT,
BY DR. KEEN.

My part in this joint paper will concern chiefly the surgical treatment of hypernephroma. Dr. G. E. Pfahler, who referred one of the cases to me has kindly consented to consider the symptomatology and diagnosis, and Dr. A. G. Ellis, who has examined not only the specimens from the two cases herewith reported, but also another, a postmortem specimen, to consider the pathology.

The term hypernephroma is so recent that it does not even appear in Morris' "Surgical Diseases of the Kidney and Ureter," the preface of which is dated May, 1901. It was first employed, I believe, by Birch Hirschfeld,¹ in 1896.

The term is applied to tumors of the suprarenal gland and is derived from a Greek form of the Latin name of the suprarenal gland. The Greek form is adopted in order to correspond etymologically with the Greek termination "oma," indicating tumor. Küster uses also the name, "epinephroma," a term of similar origin.

* Read before the College of Physicians of Philadelphia, November 2, 1904.

Such tumors arise from the adrenal tissue, whether in the normal position of the adrenal (*i. e.*, suprarenal gland) or as aberrant "rests." Prior to 1883 these tumors were called by many different names—lipoma, sarcoma, adenoma, angioma, angio-sarcoma, adeno-carcinoma, myxoma, endothelioma, etc. In the two cases here reported I did not recognize their real character by the naked eye even after they were removed; but believed them to be in the first case a sarcoma, an opinion in which Professor Weir concurred, and, in the second, a possible tuberculosis or sarcoma of the kidney.

Grawitz,² in 1883, was the first to recognize their real character as arising from the adrenal or hypernephric tissue, the title of his paper being "On the So-called Renal Lipomata."

It has been stated repeatedly that they are very rare. The statement should rather be, that, up to the present time, they have rarely been recognized, and they are much more frequent than we have heretofore supposed. Bevan even says they are the most common form of malignant tumors of the kidney and the same statement is attributed to Israel. It is not surprising that they should be frequent when we remember the wide distribution of supernumerary adrenals or "rests" of the adrenal tissue. These have been discovered in many parts of the body; in the solar and renal plexus; under the capsule, or in the substance of the kidney, or in the perinephric tissue; in the broad ligament; along the spermatic vessels; in the testicle and ovary; in the liver, the mesentery, and the inguinal canal. This is not to be wondered at when we remember that in the embryological development of the suprarenal gland, it is in very close physical connection with the mesonephros or primitive kidney, and the sexual organs. In fact, Holmes³ states that "rests" of such tissue can be discovered in various parts of the genito-urinary tract in 90% of all postmortems.

The surgical prognosis of such tumors varies greatly. Some of them never manifest any malignancy, while others are exceedingly malignant, so that, as Ramsay has pointed out, the average duration from the onset of the first symptom until death was from 6.7 months to 10.6 months, the shortest duration being six weeks and the longest three years. This is a much more malignant course than usual in other malignant growths. Happily in neither of the cases which I report tonight is there any apparent malignant tendency. In Case I, nearly

four years have passed since the operation, and the patient's health is excellent; in Case II, nearly 11 months have passed since operation, and the patient is in better physical condition than ever before in her life.

The malignancy is shown either by local extensive invasion not only of the kidney, but of neighboring organs; or by metastasis. Kelly and Bierring and Albert⁴ have called attention to the fact that metastasis not uncommonly occurs by reason of the invasion of the renal vein by such tumors. In fact, in several cases there has been even thrombosis of the vena cava itself. This invasion of the venous circulation readily accounts for such a case as is reported by Clairmont,⁵ in which the recurrence was in the bronchial lymphatic glands. In view of this possible mode of metastasis, the latter authors properly call attention to the importance of not handling the tumor roughly, either before or during the operation, and of tying the vein at as early a stage of the operation as is possible.

It is very doubtful whether in most cases a proper diagnosis can be made prior to operation, hence, as a rule, the operation must be an exploratory one, and only carried to completion in case the tumor can be removed in its entirety. If such extensive adhesions are found as to prevent entire removal, or if metastasis to other organs be discovered when the abdomen is opened, the operation should be abandoned. The operation does not differ from an ordinary nephrectomy either by the abdominal or the lumbar route, or a combination of both, as is so warmly commended by Morris. If the tumor is very large, it may be desirable even to resect the twelfth or the eleventh and twelfth ribs, though this will only very rarely be necessary.

CASE I.—R. J. D., aged 52, of Bethlehem, Pa., was admitted to the Jefferson Medical College Hospital, December 11, 1900. His father died at 87 of an unknown cause; his mother of some intestinal trouble; one sister of tuberculosis. The only illness that he remembers is an attack of typhoid 20 years ago.

Three years ago he suddenly had an attack of hematuria at night. The next morning, while at his work, severe cramp-like pains commenced and lasted for three days. They were so severe that they were only checked by the free use of morphin. The pain radiated from the kidney to the head of the penis. He had no further attacks for a year, when a second one, less severe than the first, occurred. About this time he noticed a tumor below the border of the right ribs. This was freely movable, so that he could himself push it up under the ribs and down into the right iliac fossa. He has had a great deal of pain at irregular intervals. During the last two weeks the pain had greatly increased. He had passed blood at intervals ever since

the disorder began. Within the last two weeks especially he has been troubled with almost constant and severe hematuria, and on one occasion had to be catheterized, when one and a half ounces of bloody urine with many clots was removed. The presence of the clots often produced trouble in voiding the urine. He usually had to rise two or three times during the night. Rest relieved almost all the symptoms; exercise increased them.

On examination I found a tumor extending from the median line to the flank and from the costal border to the crest of the ilium. It was only slightly movable. It measured 12 cm. vertically and 8 cm. horizontally. The right half of the abdomen measured 35.5 cm., the left 34 cm. On palpation, pressure was felt reciprocally, anteriorly, and posteriorly. Heart and lungs were normal. The urine showed a reddish, flocculent deposit, about 10%, in the specimen examined, but without clots; specific gravity, 1.019; acid; albumin, $\frac{1}{10}$ moist layer; no sugar; urea, 1.8%; by the microscope a small amount of amorphous urates, a few squamous epithelial cells, and a large quantity of blood cells, but no tube casts or crystals; no tubercle bacilli were demonstrable by stain.

Operation in my clinic, December 19, 1900. Professor Robert F. Weir, of New York, had kindly consented to conduct my clinic on this day, and operated upon this patient with my assistance. So soon as the abdomen was opened both of us believed that we had to deal with a sarcoma of the kidney. The outer layer of the mesocolon was incised and the kidney delivered and removed: the pedicle was tied with a continuous suture. The wound was then packed with iodoform gauze and only partially closed. On the sixth day the stitch was removed loop by loop without hemorrhage. The patient was discharged February 18, 1901, in good health, with the exception of a very small sinus, which, undoubtedly, would heal spontaneously in a few days. The day after the operation his temperature rose to 101° and fluctuated from 100° to 101° until the fifth day, when it became normal.

October 15, 1904, I had a letter from him, saying that he is in excellent health, with no evidence of any recurrence after nearly four years.

Dr. Ellis reported as follows (Laboratory No. 1,415):

Two tubes of glycerin agar were inoculated with urine; in 24 hours an abundant growth was demonstrable, grayish-white in color and extending over the whole surface of the medium. There was also abundant gas production noticed in the tubes. Spreads were made and stained with Löffler's methylene-blue and by Gram's method.

Microscopically numerous bacilli were demonstrable, 1 micron to 3 microns in length and .3 microns in thickness arranged and occurring for the most part in pairs and also singly. They decolorized by Gram's method. Together with this organism there is seen another bacillus, 1 micron to 2 microns in length, .8 microns in thickness occurring mostly singly, having rounded ends and more or less oval in shape and staining by Gram's method, corresponding to *Urobacillus pasteurii*. Cocci are also seen which are identical both morphologically and tinctorially with staphylococci.

Diagnosis.—*Bacillus coli communis*; *Urobacillus pasteurii*; *Staphylococcus pyogenes albus*.

Dr. A. G. Ellis also made the following report upon the kidney :

CASE I. (Laboratory No. 1,416.)—The specimen is a kidney strongly resembling the spleen in shape and 13 cm. by 10 cm. by 9 cm. in dimensions; the weight is 520 gm. The plane surface is covered by a rather firm, thick, smooth capsule, brownish-red in color, containing numerous dilated vessels. An oval depression measuring 5 cm. by 3 cm. and corresponding to the renal pelvis, extends diagonally across this surface; the margins of this depression are rounded. Projecting from it is a mass of fat and also several nodules, each 2 cm. in diameter and dark blue in color. The convex surface of the specimen presents a markedly lobulated condition which includes bossed elevations 3 cm. to 5 cm. in diameter; distinct nodules, 1 cm. to 2 cm. in diameter and from 1 mm. to 5 mm. in height, some presenting a cauliflower appearance; and, finally, mere granular points may be distinguished. These varied projections are entirely subcapsular, the capsule in no way differing from that covering the plane surface. The color variations of the nodules are remarkable, varying from pale gray to deep blue or red, all shades between these being represented. In consistency, some of the nodules are soft, as though cystic, while others are quite firm. Incision of the specimen meets considerable resistance, and exposes surfaces of varying composition. Medulla and cortex can be differentiated only at the larger end, where there is an area of renal structure 5 cm. by 2 cm. by 2 cm. In this is seen one pyramid, the overlying cortex varying from 3 mm. to 10 mm. in breadth. This area is separated from the remainder of the surface by a band of dense white fibrous tissue from 0.3 cm. to 1 cm. wide, and extending from end to end; from this, narrower bands of varying width project into the surrounding tissue in every direction, dividing the surface into irregular alveoli. These bands are especially adherent to the capsule of the specimen, and extend deeply into what is apparently the renal pelvis. The enclosed areas or alveoli contain finely granular, softened masses, ranging in color from grayish-pink to red or blue. In a few, the contents are yellow and firm. The specimen was fixed in Heidenhain's solution, dehydrated, cleared and embedded in paraffin; sections were cut and stained by hematoxylin, with the addition of eosin or Van Gieson, toluidin blue, and Mallory's reticulum stain.

Microscopical examination shows the tumor to be divided into various sized, irregularly circular or oval alveoli by broad bands of dense fibrous tissue, continuous with the capsule at certain points. In these bands are small areas resembling in miniature the alveoli enclosed by the stroma. The alveoli proper are occupied in part by a reticulum of fibrous tissue which transmits blood vessels. Certain of these vessels are quite large and possess relatively thick walls, others are capillary in size and are bounded by endothelial cells only. The former, in many instances, appear to be dilated, though at such points they contain little or no blood. Lining the spaces formed by this reticulum are large cuboidal or polygonal cells. These are placed on the fibrous stroma, or in the case of capillaries, on the endothelium forming their walls, giving in the latter instances the appearance of double rows or columns. Each cell possesses a single large deeply-staining nucleus placed centrally or near the base of the cell. Nucleoli are usually, but not always, conspicuous. The cytoplasm in the greater number of

cells stains faintly. It is represented largely by vacuoles that undoubtedly are spaces formerly occupied by fat. Some of the smaller reticular spaces are almost filled by these cells, the free ends closely approaching each other. Larger spaces contain detached cells and also red blood cells, in many of the alveoli blood being present in such quantities as to become the predominant feature.

Diagnosis.—Hypernephroma of right kidney.

CASE II.—Mrs. W. H. P., aged 54, of Philadelphia, was first seen in consultation with Dr. G. E. Pfahler, on December 12, 1903. Her father died of carcinoma of the face, and her mother of carcinoma of the breast. She has been more or less of an invalid for many years. Two years ago she suffered from marked indigestion, but made a fair recovery. In the early winter of 1902 she suffered from two accidents, but it is not certain that they injured the kidney. In one she was thrown from a carriage; in the second she fell from a stool upon which she was standing. After this second accident she kept her bed for several days.

On December 12, 1902, after exertion connected with a social function, at which she ate some chicken salad, her present illness began with marked gastro-intestinal symptoms, such as nausea and occasional vomiting, alternate diarrhea and constipation, and vague abdominal pains, accompanied with languor, progressive weakness, and anemia.

In January, 1903, a small polyp was removed from the cervix uteri by Dr. Elizabeth L. Peck. Dr. Peck at the same time discovered a movable tumor in the right lower abdomen, which she thought was probably a floating kidney. Dr. Pfahler was first called to see her early in November, 1903, and immediately took careful skiagraphs of the abdominal tumor. In the skiagraph the shadows were first thought to be gall-stones, but later Dr. Pfahler was disposed to think that the tumor was a kidney with a suspicion of three stones in it.

The blood examinations were as follows:

	Erythrocytes.	Leukocytes.	Hemoglobin.
November 23.....	3,920,000	12,000	40%
November 30.....	4,200,000	10,000	41%
December 14.....	4,690,000	8,000	42%

The urine was negative. She had never had an attack of hematuria. There was some mucus in the stools.

A few days prior to my examination she had vomited some undigested food, in which Dr. Pfahler found no free HCl. Owing to her great weakness he had not administered a test-meal. In the region of the pylorus there seemed to be a painful spot, with possibly increased resistance, but this was rather vague. She has never had renal colic. Her pulse has usually been from 80 to 90; her temperature from 100° to 102° of late. Her normal weight was 113 pounds, but this had fallen by November to 97 pounds, and when I saw her December 12 it was probably below 90 pounds. Her weakness had progressively increased so that she was very feeble.

On examination I found a rather slender delicate woman, evidently very ill, but who faces her grave condition with great equanimity, and has made up her mind that an operation is necessary and shall be done. As soon as the abdomen was exposed a tumor was perceptible to the sight on the right side of the abdomen, extending from the right iliac fossa to the border of the ribs, and from near the median line into the right loin.

Reciprocal pressure was felt in front and behind. It was not particularly painful, and was fairly movable. No tumor about the pylorus or gall-bladder could be made out, nor was there any great sensitiveness. My diagnosis was a kidney enlarged to nearly, if not quite double its normal size by the presence of a tumor. I advised an abdominal section. The evidence for disease of the stomach was not convincing, but if there were any serious condition found, it would have to be operated upon.

Operation.—December 16, 1903, by an incision in the right semilunar line. As soon as the abdomen was opened, I drew out the stomach, which seemed to be entirely normal. In the kidney a large tumor was perceptible just above its middle. It was lobulated, and in my opinion probably a sarcoma. The kidney was delivered through an incision in the outer layer of the mesocolon. The pedicle had to be tied in several sections; one enormous renal vein, at the upper part, the size of a finger, gave me considerable trouble, and required three ligatures before it was completely secured, the final one being very near to the vena cava. As a further precaution against later hemorrhage, I packed some iodoform gauze over the stump. The distal end of the ureter was tied, cauterized with pure carbolic acid, and dropped. The mesocolon was then closed, except where the packing found its exit, and the operation terminated.

The operation was done on a hot water mattress. During the operation, Dr. A. B. Craig infused a quart of saline solution with a drain of adrenalin, 1-1,000. In spite of her great weakness, whether due to these precautions or not, there was practically no shock after the operation, the temperature only falling from 99.2° to 98°, and the pulse rising from 109 to 118.

Blood examination on December 30:

Erythrocytes	4,910,000
Leukocytes	8,800
Hemoglobin	42%

On the third day the packing was removed. Her temperature never rose above 99.6°, saving at 4 p. m. of the day of the operation, when it rose for once only to 103.2°, and she made an uninterrupted recovery.

The following table shows the secretion of urine from the left kidney:

First 24 hours.....	9 $\frac{1}{2}$ ounces
Second " "	15 $\frac{1}{2}$ "
Third " "	12 $\frac{1}{2}$ "
Fourth " "	13 $\frac{3}{4}$ "
Fifth " "	16 $\frac{1}{4}$ "
Sixth " "	12 $\frac{1}{2}$ "
Seventh " "	20 $\frac{1}{2}$ "
Eighth " "	14 $\frac{1}{2}$ "
Ninth " "	16 $\frac{1}{2}$ "

To all of these amounts should be added more or less urine passed with the stools. Two culture tubes inoculated from the kidney showed no growth.

I first thought that the tumor was a sarcoma. Later, on making a section of it, I was inclined to think it was possibly tuberculous. The histological examination by Dr. Ellis, however, as he will explain, showed it to be a hypernephroma.

By February 15, 1904, two months after the operation, she had gained 30 pounds in weight.

On January 26, 1904, the blood examination showed:

Erythrocytes	4,940,000
Leukocytes.....	8,600
Hemoglobin.....	56%

By May 14, 1904, her hemoglobin had risen to 70%.

On October 20, 1904, I saw her in blooming health. Her weight had increased to 136 pounds as contrasted with less than 90 pounds 10 months before. Indeed she asserts that she is in better health than she has ever been before. The urine varies from 38 ounces in hot weather to 60 ounces in cold weather. The average is about 46 ounces.

Dr. Ellis made the following report upon the kidney:

CASE II.—(Laboratory, No. 2,546.) The specimen consists of a kidney 11 cm. long, 5 cm. wide, and 3.5 cm. in maximum

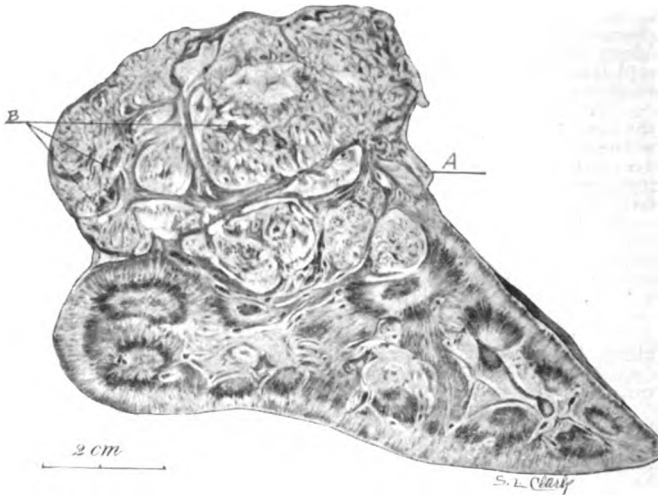


Fig. 1.—Hypernephroma. Case II. A, Capsule of kidney extending over tumor; B, areas of hemorrhage.

thickness. The weight is 298 gm. The organ shows no conspicuous gross lesion, except on the posterior aspect of the upper half, where there is a projecting tumor, irregularly globular in outline, measuring in its greatest diameter 7 cm. It projects beyond the surface of the kidney a distance of 4 cm. The tumor is covered by a capsule, which is apparently an extension of the capsule of the kidney. It is very thin, translucent, and contains numerous small, distended blood-vessels. Broadly speaking, the surface of the tumor is fairly smooth, though it presents several rounded elevated areas, varying from 0.5 cm. to 2 cm. in diameter. These areas have a maximum elevation of 0.6 cm. and merge gradually with the surrounding

surface. They are much softer than the intervening tissue, which is quite firm, though readily compressible by the finger. The color of the tumor mass beneath the capsule is distinctly yellow. A few punctate dark areas resembling small extravasations of blood are scattered over the surface. Externally, the tumor is sharply differentiated from the substance of the kidney and a mesial incision, which has been carried through the mass into the renal pelvis, shows the entire tumor to be thus clearly outlined. (Fig. 1.) Both cortex and medulla of the kidney have been usurped by the growth, which extends to the renal pelvis, without encroaching upon or notably projecting into that structure. The depth of the tumor as measured from

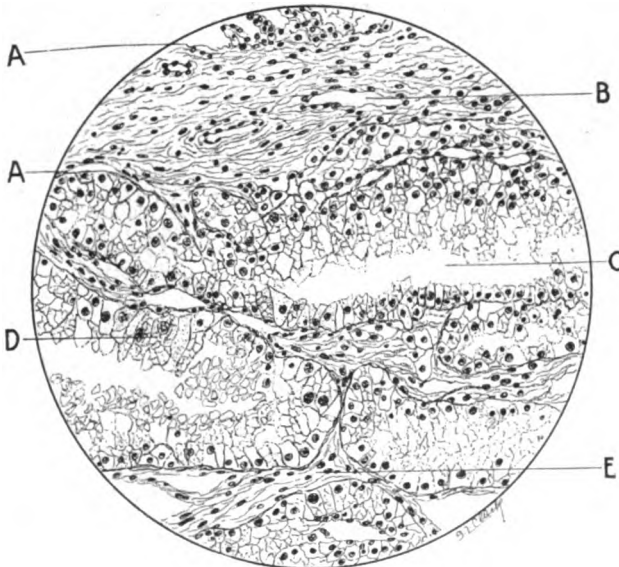


Fig. 2.—Section of hypernephroma, showing capsule (Case II). A to A, capsule; B, blood-vessel in capsule; C, alveolus surrounded by polyhedral cells, many of which are columnar and possess the general characters of the cells found in the adrenal cortex; D, typical spongiocyte; E, connective-tissue reticulum.

the external surface to its termination at the pelvis of the kidney is 7 cm. The upper border of the growth is, at its junction with the surface of the kidney, 2 cm. from the extreme upper end of that organ, but its free extremity projects beyond the attachment until the outer portion is even with the margin of the kidney. The incised surfaces of the growth are yellow in color. They are marked out into variously sized circular or oval areas by narrow bands of grayish tissue, presumably fibrous in character. These areas exhibit pronounced bulging. Minute reddish points are seen dotting these surfaces, ap-

parently marking the situation of severed blood-vessels. Further incision of the mass reveals the presence on the surfaces of darker areas 0.5 cm. to 1 cm. in diameter. A few areas of softening are noted. The entire tumor mass, on its incised surfaces, is soft and very friable.

Slightly below the center of the posterior surface of the kidney and a little internal to the common border, at a point 2 cm. from the margin of the tumor described, is a yellowish, slightly elevated nodule 0.5 cm. in diameter. It is immediately beneath the capsule of the kidney and is quite dense in texture. This nodule was removed entire, with the surrounding portion

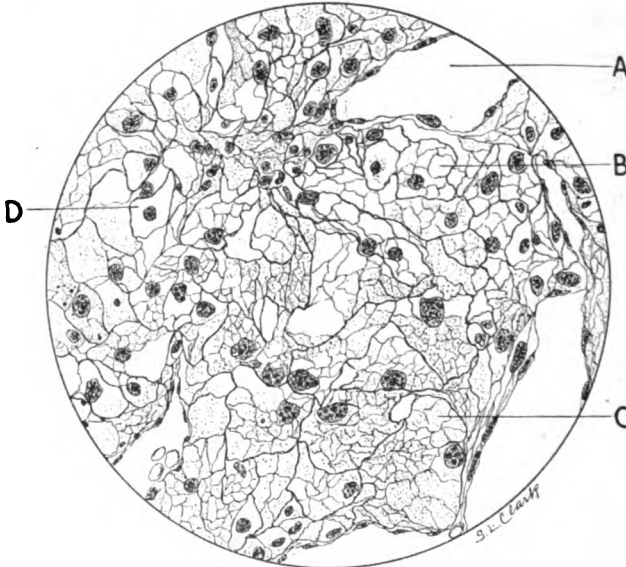


Fig. 3.—Section of hypernephroma, showing character of cells. Same section as Fig. 2 (Zeiss 2 mm. homo. im.). A, blood-vessel; B and C, spongocytes. In the upper cell (B) the intraprotoplasmic spaces appear empty; the corresponding areas in the lower cell (C) contain faintly acidophilic fine granules. D, similar cell, with structureless clear protoplasm.

of the kidney, for further study, hence its depth of penetration was not at this time noted.

Inoculations were made and cover-glass spreads prepared from the tumor; part of the latter were fixed in absolute alcohol. Half of the specimen was preserved by Kaiserling's method. The other half was fixed principally in Bensley's fluid, but small portions were also placed in absolute alcohol and in 10% formalin.

Examination of spreads stained by methylene-blue shows them to contain a variety of cells. Polymorphonuclear leukocytes are quite numerous as are also lymphoid and hyaline

cells. In addition to these are large polyhedral cells ranging from 12 microns to 40 microns in diameter. The cytoplasm is finely or coarsely granular. The nucleus is large and usually single, though occasionally two nuclei are noted and in one cell, four are present. Some of the nuclei stain deeply, but many are but little darker than the cytoplasm. One or more nucleoli are usually present. A few of these cells, particularly the smaller ones, contain one or more vacuoles. In certain others a clear space separates the nucleus from the cytoplasm. Inoculations on agar yielded no growth.

The fixed portions of the tumor were embedded in paraffin and sectioned. Sections were stained by hematoxylin and eosin, hematoxylin and Van Gieson, toluidin blue, Mallory's reticulum stain, and by specific stains for glycogen.

Microscopical examination of the sections shows the following characters: Sections including both the kidney substance and tumor show these two structures to be separated from each other by a distinct zone of fibrous tissue. This zone is quite wide and shades off gradually into the kidney substance proper, appearing to be a condensation of the renal tissue, with some added fibrosis, rather than a true capsule of the tumor. The structure of the tumor at this point is that of an exceedingly scanty, almost filamentous, fibrous stroma or reticulum, which ramifies in various directions as long bands, to each side of which are attached large cells, or form variously sized alveoli lined by similar cells (Fig. 2). These cells vary in size but the majority are extremely large. They are cuboidal or columnar in type and contain round, fairly deeply staining nuclei, situated usually near the middle of the cell. The cytoplasm is very loose in structure and stains indifferently. It contains in many of the cells numerous clear or translucent areas that suggest the presence of fat, but which do not have the regular, clear-cut outline usually presented by distinct globules of that material. In many areas these cells are but one layer in depth, but other portions are made up of alveoli practically filled by several layers of them. In such areas the limiting membranes of the cells are the most conspicuous feature, forming an irregular network in which is seen the slightly granular, shadowy cytoplasm. (Fig. 3.) Many of these cells contain no demonstrable nucleus. Portions of the tumor are quite compact, while others possess an exceedingly scanty network of stroma and cells, the large spaces thus formed containing in some instances blood, in others detached tumor cells, both showing various degrees of cytolytic change. The parts of the tumor described resemble, in general structure and character of the cells, the zona glomerulosa of the adrenal gland, showing here, of course, cellular proliferation and also degenerative changes. In other sections are seen areas made up of columns of cells forming a network in the interstices of which are capillary blood-vessels. These cells are much smaller than those previously described, containing vesicular nuclei and clearly defined fat spaces. The similarity of these areas to the zona reticularis of the adrenal is very striking. Sections stained for glycogen by the iodine method show numerous variously sized granules or droplets of that material in the large cells of the tumor.

The kidney shows granular changes in the epithelium of the tubules, accompanied, in some areas, by considerable desquamation. Slight recent hemorrhages into the tubules or tufts are occasionally noted, but are not at all conspicuous. A few granular tube casts are in situ. The capsule of the organ is

slightly thickened and small areas of beginning fibrosis immediately beneath it are observed. The conspicuous fibrous transformation in the vicinity of the tumor has been previously mentioned; parenchymatous change is also more noticeable as the tumor is approached.

Sections through the small nodule in the kidney, mentioned in the gross description, show it to be beneath the thickened renal capsule. It is made up of a loosely arranged network of fibrous tissue enclosing spaces which, in the central part of the mass, contain cells resembling to some extent those in the large tumor. Dense accumulations of lymphoid cells are also present. Although it cannot be definitely stated that this is a metastasis from the larger tumor, it is reasonable to suppose that such is the true nature of the small nodule. It is not sharply demarked from the adjacent tissue, possesses the semblance of a capsule at points only, and shows, equally with the larger mass, such evidences of growth as to indicate that both are progressing at about the same rate; if any difference can be inferred (for inference is all that is possible upon this point), the smaller tumor would appear to be the more rapidly growing of the two.

Diagnosis.—Multiple hypernephroma of right kidney; slight chronic diffuse nephritis.

By the kindness of Professor Coplin, Dr. Ellis had the opportunity of examining a third specimen obtained postmortem.

CASE III.—The specimen was obtained at autopsy upon the body of a man aged 43, the pathologic diagnosis being: Chronic adhesive pleuritis, arterio-sclerosis, chronic interstitial nephritis, chronic interstitial pneumonia, hypernephroma of left kidney, arterio-sclerotic softening of right cerebrum.

The left kidney was small, lobulated, and possessed an adherent capsule. On the convex border, just above the middle of the organ, was a slightly elevated, nearly circular nodule 1 cm. in its longest diameter. It was yellow in color, and sharply differentiated from the surrounding tissue. The surface of the nodule was roughened by small projections, giving it a wart-like appearance. Incision showed the tumor to be almost spherical in outline and slightly more than 1 cm. in diameter.

Microscopical examination of sections from the specimen shows an encapsulated tumor situated immediately beneath the capsule of the kidney. The latter structure where it surmounts the tumor is considerably thickened and elevated. In addition to the general elevation, caused by the location of the growth, the capsule of the latter sends outward several projections that produce irregular secondary elevations of the kidney capsule, and impart to it a papillomatous appearance.

The capsule of the tumor is a broad band of fibrous tissue, which, throughout the larger part of its extent, presents two fairly distinct, but not sharply delimited zones. The outer is composed of rather dense tissue, containing but few blood-vessels and cells; the inner zone is not so dense, and shows more or less conspicuous invasion by tumor elements. This is particularly true of the part bordering the kidney, where evidence of extension of the growth is most marked. Here, even the outer zone is extremely cellular, shading gradually into kidney

substance undergoing progressive fibrous transformation. The larger blood-vessels in this area are the site of obliterative endarteritis. Into this extending capsule, tumor elements are well advanced. At several points are quite large spaces better considered in connection with the tumor itself. Scattered throughout a large part of the capsule and extending into the stroma of the tumor, are granules and irregular collections of golden-brown pigment, both intra-cellular and extra-cellular in location.

The tumor proper is composed of a fibrous reticulum enclosing variously sized cell-lined spaces. The bands of the reticulum transmit capillaries and vary considerably in thickness; some consist of but little more than the endothelial wall of the capillary, others are distinct, though narrow, fibrous bands. The reticulum does not extend inward from the capsule as prominent narrowing and dividing trabeculas, but, as stated in the description of the capsule, presents more the appearance of impinging upon and invading the inner portion of that structure. The cells lining the spaces of the tumor are large and usually polygonal in outline. They are attached perpendicularly to the reticulum, and where the latter is most scanty present the appearance of double rows or columns separated but slightly by the capillary wall. The nucleus is usually situated toward the center of the cell and reacts well to chromatin stains; the cytoplasm stains very faintly, and in most of the cells contains large fat spaces. The spaces enclosed by the reticulum of the tumor vary in size from those essentially filled by the lining cells up to cavities 2 mm. in diameter. The smallest spaces contain detached cells of the type described and a few red blood cells; the large cavities are nearly filled with blood, and also contain desquamated cells in various stages of disintegration. A few of the better preserved cells contain pigment similar to that described in connection with the capsule. The spaces previously mentioned as located in the capsule are similar to those just described, and are evidently extensions of the growth; the largest is 0.5 mm. in diameter.

The histology of that part of the kidney immediately bordering the tumor capsule has been described in connection with the latter structure. Further from the tumor, and presumably uninfluenced by that body, the renal cortex shows a decided increase in connective tissue, with hyalo-fibrous transformation of the glomeruli. The tubular epithelium is granular, fatty, and desquamating.

Diagnosis.—Hypernephroma of left kidney; chronic diffuse nephritis.

SYMPTOMATOLOGY AND DIAGNOSIS, BY DR. PFAHLER.

As Dr. Keen has indicated there is but one method of treatment, and that is operation; and the earlier it is performed the greater are the chances of complete recovery. All, then, depends upon an early diagnosis. With the object of working out the symptomatology and diagnostic factors, and at the suggestion of Dr. Keen, I have reviewed the literature upon the subject, have made an

analysis of the clinical histories, and have tabulated the symptoms of the cases reported, including our two cases.

The great majority of the reports upon this subject contain only the description of the pathological nature and tendencies of these growths. In this collection, I have included only undoubted cases of hypernephromas in which the clinical reports contained all of the symptoms and observations that were noticeable; but have not included the cases reported in which the symptoms were produced by metastatic growths. In very few were the clinical histories complete, nor were all of the methods of investigations used that were at our command. Until all such methods of investigations have been used, we have no right to claim that a diagnosis cannot be made. I have collected and tabulated 26 cases. (See table.) The three most important symptoms or diagnostic factors connected with the disease clinically are hematuria, renal colic, and the detection of a tumor. All of these may occur together, any one may occur alone.

The most constant of these is *hematuria* which is usually the first symptom complained of by the patient. In 63 cases studied from this point of view by Albarran,* it was the first symptom in 36. It occurred at some time during the course in 58 out of 77 cases, or in 75%. Hematuria occurred alone in 4 cases, with a tumor in 28, with pain in 4, and with pain and tumor in 22. In the cases collected by me, hematuria was present in 19 out of the 26. It was associated with pain in 14, and with tumor in 15 cases.

It is probably only present when the kidney itself is involved, but, as Dr. Ellis will show, the kidney is involved in nearly all cases, and therefore this distinction is of little practical importance. Usually the hemorrhage begins without apparent cause, and at times while the patient sleeps; but in three cases it seemed to be excited by traumatism or exertion. In one case it was caused by direct traumatism to the lumbar region; in another by the lifting of a heavy barrel; and in a third case it occurred at the end of a race, associated with fainting. In one of our own cases (No. II) trauma may have been a factor in the causation of the disease. It is usually sufficient in amount to form clots, and may amount to a pint or more; and it may be passed as almost pure blood. Ureteral clots are often present.

Hematuria may be almost constant for several months, and then be entirely absent for several months.

It usually occurs at intervals, and lasts but a short time. Plummer⁷ mentions a case in which hematuria occurred only once, 14 months before operation. Morris⁸ also reports a case in which hematuria only occurred once, two years before the operation. In seven of the 26 cases there had been no hemorrhage during the entire course, and no urinary symptoms. This was true in one of our cases (No. II) and in this case half of the kidney structure was involved by the growth. Therefore the absence of hematuria does not indicate that the kidney itself is free from growth.

Pain.—The usual form of pain is that which is usually described as renal colic; but it may be a mere dragging sensation, or dull pain in the lumbar region, such as occurred in the cases of Thorndike and Cunningham.⁹ Morris mentions two cases in which the pain occurred in the region of the gall-bladder and lumbar region, respectively, and radiated toward the right shoulder.

The pain usually occurs with the hematuria, and in such instances may be due to the formation and expulsion of clots from the ureter. It may occur without hematuria, such as was noted in one of Bierring's,³ and two of Lubarsch's¹⁰ cases. In the study of this point by Albarran, pain was the first symptom in 20 out of 63 cases. Of these 20 cases, it occurred alone in 14, with blood in 5, and with tumor in 1. In 77 cases, pain was present at some time during the course in 32. In my series it was present in 19 out of the 26 cases.

Tumor.—A tumor may be discovered by the patient before any other symptoms have been produced. It was the first symptom in 12 out of the 63 cases studied by Albarran. The same author found it present at some time during the course in 69 out of 77 cases, or in 89%. In my series of 26 cases it was detected in 21. As a rule the tumor is detected after other symptoms have become manifest, and the interval between the earliest symptoms and the discovery of the tumor may be several years. In size the tumor varies, but may reach that of a child's head. Out of the 26 cases 4 were so described. The tumor was movable in 12 of the 26 cases. This mobility varies from a slight movement with respiration to very free movement, and this forms a very valuable point in the differential diagnosis. Tenderness was elicited in 6 of the 26 cases.

Location: The tumor was found upon the right side in 18 of the 26 cases.

General Symptoms.—The general symptoms consist chiefly of a marked asthenia, emaciation, and languor or depression. These symptoms were present in 18 of the 26 cases. The color of the skin is usually described as being pale. In only two was it described as cachetic, and in none of them was it found to be bronzed. Gastro-intestinal symptoms were complained of in 5 cases. In one of our cases (No. II) it was the chief complaint.

The *blood* has been examined in only 4 cases, and in one of these only the leukocyte count was made. In the 4 cases the leukocytes varied from 6,000 to 12,000. The hemoglobin was comparatively low, once as low as 25%. In one of our cases it was 41%, while the erythrocytes were 4,200,000, the leukocytes were 12,000, and the differential count was normal. We had therefore in this case the blood picture of chlorosis.

The examination of the *urine* was reported in 13 of the cases, but except when it contained blood, it was practically normal.

The *age* was given in 22 cases. The oldest patient was 73, and the youngest 38, the average being 52. Hypernephroma therefore, as a rule, appears to be a tumor belonging to middle and advanced age. Albarran says that it is rare below 40, and after 60.

The *sex* was mentioned in 24 of the 26 cases. It was found 13 times in the male, and 11 times in the female. This point was studied by Lubarsch in 28 cases, 19 of which were in the male. This disease therefore seems to occur rather more frequently in the male.

Heredity.—The family history was mentioned in only 6 of the 26 cases. In 3 of these 6 there was a distinct history of carcinoma in the parents.

Duration.—The duration of the symptoms varied from 15 weeks to 8 years, or an average of 2 years and 3 months.

Grawitz and Strübing⁷ report a case in which a tumor was present in the region of the kidney 5 years, J. Israel¹¹ one 8 years, and Beneke¹² one 10 years, while Askanazy¹³ reports a case in which the tumor was discovered early in youth, then lay dormant twenty some years, and produced symptoms at the age of 53.

Hypernephroma therefore may be a slowly growing tumor. This should not, however, become an excuse for delay in operation, because at any time an intercurrent affection may cause rapid progress of the disease, followed by metastases. This was noted in two

cases after an attack of influenza. ~~One of these cases~~

growths, regarding the histogenesis of which there exists difference of opinion, and even with regard to carcinoma

General Symptoms.—The general symptoms consist

body, followed by micrometastases. This was noted in two

cases after an attack of influenza. One of these cases was reported by Lubarsch.

Special examinations were made in 9 cases. A cystoscopic examination was made in 3 cases, and in each showed blood coming from the ureter of the diseased side.

A röntgen-ray examination was made in 3 cases. In 2 it excluded stone. In one of our cases, a shadow of the tumor and kidney was shown, and in the general outline more dense shadows were obtained which corresponded to the nodules of the tumor. In a case reported by Lubarsch, an examination under ether, which was made three months before a tumor could be felt, gave increased resistance over the kidney. In one of Robson's¹⁴ cases the colon was inflated, and the tumor was pushed up toward the liver. In a case reported by Morris, a varicocele had developed upon the affected side, which was found to be due to a distortion and dilatation of the spermatic vein as it passed over the tumor.

Diagnosis.—The diagnosis of these tumors is, of course, very difficult, since we have no pathognomonic sign or symptom, but I believe that it can be made in some cases by a careful consideration of the symptoms, coupled with a complete examination. The diagnosis simply of tumor of the kidney was made in a number of the cases reported, but it is most desirable that a correct diagnosis should be reached before any palpable tumor exists, and that an exploratory operation should immediately follow the diagnosis.

The diagnosis can only be made by the method of exclusion. Time and space will not permit of a review of the methods that may be used, but a study of the foregoing table will give an idea of the points to be investigated directly.

Having excluded the other causes of hematuria and renal colic, and having detected or suspected a tumor of the kidney in a patient of advanced life, especially if it occur upon the right side in a male and is freely movable, we are justified in making a diagnosis of hypernephroma, and in advising an exploratory operation.

PATHOLOGY, BY DR. ELLIS.

The terminology of tumors of the adrenal and kidney is still in a state of considerable confusion. This is particularly true of certain adenomatous and lipomatous growths, regarding the histogenesis of which there exists difference of opinion, and even with regard to carcinoma

and sarcoma all authorities are not fully in accord. Grawitz, in 1883, to the views then held, introduced a conflicting element by his assertion that a group of the smaller tumors of the kidney, currently recognized under the name of lipoma, were in reality derived from aberrant adrenal glands. For them he suggested the name of *strumae lipomatodes aberrati renis*. New interest in the subject was immediately aroused and the results of numerous investigations were soon published. In general, the views of Grawitz were supported, though dissenting opinions were by no means few in number. This has remained the status of the question up to the present time, although the opponents of the views of Grawitz have steadily lost ground as carefully studied cases have increased in number. To these tumors Birch-Hirschfeld, in 1896, applied the name of hypernephroma, a term now most often employed, though by some they are designated simply as adrenal tumors.

Histogenesis.—It is not my purpose at this time to enter into a lengthy discussion of the histogenesis of these tumors. Those who wish to investigate this phase of the subject are referred to the admirable work of Kelly¹⁵ for a critical summary of the earlier writings as well as the findings of careful original studies. Among the most extensive recent contributions are those in the works of Hoche and Albarran and Imbert. It should be said, as previously intimated, that the literature of the subject, since Kelly's paper appeared in 1898, is principally in the nature of reports of additional cases, lending weight to the original views of Grawitz. Apparently conflicting opinions are, for the most part, due to differences in histologic interpretation rather than dissent to the original proposition. Hoche,¹⁶ after carefully reviewing the subject, is unwilling to admit that the theory of Grawitz is absolutely demonstrated, but says it is sufficiently established for one to believe, until proved to the contrary, that certain intrarenal tumors originate in adrenal tissue.

Albarran and Imbert⁴ regard the reasons given by various writers and summarized by them, as being fully sufficient to establish hypernephroma on a solid basis. They are convinced, however, that many tumors of the kidney, if examined by different pathologists, would be pronounced by some "epitheliomas with clear cells" and by others hypernephromas. This is due to the probability that malignant tumors with clear cells develop from aberrant adrenals, and also that neoplasms identical in appearance may take origin in the epithelium

of the kidney. The future must teach us to distinguish between the two. Albarran and Imbert recognize three varieties of lipoma or pseudolipoma of the kidney: (1) The true lipoma described by Virchow; (2) pseudolipoma or hypernephroma of Grawitz; (3) pseudolipoma of Ulrich, resulting from fatty degeneration of the epithelium lining the convoluted tubules. Tumors of the kidney in general are placed by these authors in four groups: Group 1. Tubular and papillary adenomas and carcinoid epitheliomas with the transition form of adenocarcinoma. Group 2. On the one side the benign pseudolipoma of Grawitz and alveolar adenomas; on the other side malignant hypernephromas, which include in great part the epitheliomas of clear cells. All these, with evolution benign or malignant, may come from capsular debris. It is also possible that a certain number of cancers with clear cells may originate in renal canaliculi. Group 3. Sarcomas, lipomas, and true angiosarcomas that originate from the mesodermic tissue of the kidney. Group 4. Mixed tumors originating in embryonal germs. They believe that the tumors described by Paoli, Driessen, and others under the name of endothelioma, angiosarcoma, etc., relate in part to carcinomas of clear cells, particularly to those which take their origin in aberrant adrenals.

Kelynack¹⁷ holds that but few pathologists now deny the adrenal origin of certain renal growths. McWilliams¹⁸ says "the pathogenesis of adenomas of the kidney is obscure. Some are undoubtedly of accessory adrenal origin, others arise from remains of the Wolffian body, others from isolated elements due to errors in development." Williams¹⁹ thinks "this (suprarenal) origin for certain renal tumors may be considered as firmly established as any fact in renal neoplastic pathogeny."

Kelly,²⁰ in a later article, says that most of the so-called primary carcinomas and alveolar sarcomas of the kidney are in reality hypernephromas. Bland-Sutton²¹ speaks of renal "sarcomas" arising in adrenal rests, and states there are no facts to support the assumption of some writers that renal sarcomas arise in the adrenal gland and gradually become incorporated with adjacent parts of the kidney. Morris²² observes that the microscopic characters of this group of tumors are capable of various interpretations, and what one person classifies as a typical renal tumor of accessory adrenal origin, another calls spheroidal-celled carcinoma, another endothelioma, still others epithelioma of clear cells, renal adenoma,

primary angiosarcoma, alveolar sarcoma, or lymphadenoma. Norman²² describes an encapsulated tumor an inch in diameter, half of which was within, the other half projecting from the surface of the kidney. The cells were cylindric and loaded with fat. He believes there is not sufficient evidence to support the theory of Grawitz, and prefers the explanation of Sabourin, that these tumors originate in proliferated epithelium of the convoluted tubules of the kidney.

Parodi²³ grafted adrenals from embryo rabbits into the kidney, liver and sciatic nerve of rabbits three or four months old and also into adult animals. The cortex became adherent, the medulla did not; after a time this was smothered by developing connective tissue. The morphology of the grafts in the kidney and liver led Parodi to the conclusion that adenomas of those organs assuming hyperplasia must be considered as adrenal inclusions. Neusser²⁴ says that excessive proliferation of circumscribed portions of suprarenal substance gives rise to small tumors resembling lipomas which have been termed suprarenal strumas or adenomas. They are situated in the cortex of the suprarenal capsule or more frequently in accessory glands occurring in the kidney. According to the latest views he believes they are to be considered as sarcomas of the vascular perithelium (perithelioma). Ricker,²⁵ in certain cases in which the adrenal was abnormally near the kidney, found renal tumors in the adrenal and adrenal tumors in the kidney. Of nonmalignant tumors of the kidney he describes: 1. Tubular adenomas. 2. Trabecular cystomas. 3. Those of adrenal origin.

These references might be many times multiplied, but they are sufficient to demonstrate two things: 1. The majority of writers recognize the adrenal origin of certain tumors called hypernephromas found in the kidney and elsewhere at points near to, or remote from, the adrenal gland itself. 2. The difficulty of deciding in all instances between hypernephroma and adenoma, lipoma, or even carcinoma of either kidney or adrenal; this may be assigned as one reason for the existing differences of opinion regarding renal growths in general, and the one we are at present considering in particular. Hypernephroma, then, may be defined as a tumor arising from adrenal tissue, whether in the normally situated gland or in ectopic fragments of that organ known as adrenal rests. By common usage the term is seldom applied to growths of the adrenal itself, being reserved almost exclusively for those springing from

aberrant particles of the gland. Primary hypernephroma, therefore, while usually in the kidney (96% of reported cases), is possible in widely different situations.

Embryology.—The embryology of the adrenal gland throws much light upon this frequent occurrence of ectopia of the organ. Radasch²⁷ mentions that at one time in the development of the embryo the adrenals are comparatively large and enclose nearly the whole of the kidney. As the fetal kidney is lobulated, he says it may be readily understood how small detachments of adrenal cells could, at that time, be enclosed in the interlobular connective tissue of the kidney. The development of the adrenal from the same type of tissue and in relation with the sexual glands accounts for the frequency with which fragments of the former are strewn along the paths of the latter in their descent. Radasch also states that ectopic adrenals occur in both sexes, the usual location being some point between the kidney and the descended sexual gland. They have been found in or upon the adrenal, kidney and liver, in the perirenal tissue, solar and renal plexuses, mesentery, in the region of the internal abdominal ring, in the inguinal canal, upon the spermatic cord, between the epididymis and testis, in the broad ligament, and the fundus of the uterus. Marchetti²⁸ has also found them embedded in a serous cyst of a human ovary and in the ovaries of guineapigs. The frequency of ectopic adrenals is placed by some writers surprisingly high. Imbert²⁹ says they are found in 92% of all bodies coming to autopsy, and in the kidney in 6% to 8% of cases. Holmes³ places the number at 90% of all autopsies, the bodies being found in various parts of the genito-urinary tract. Duckworth³⁰ mentions the case recorded by Pitt, in which there were four adrenals, two being on the anterior surfaces of normal kidneys, an inch from the upper end. Wynn³¹ has observed a high frequency of supernumerary adrenals in cattle. McFarland³² does not believe they are so frequent in man as in cattle. He has made a careful examination in more than 1,000 autopsies and in them has never seen a distinct supernumerary adrenal. Kelly (*loc. cit.*) found an instance of union of the adrenal bodies with the kidneys and misplacement of portions of the former within the latter. The tendency of the adrenal itself to abnormal development is shown by Flint,³³ who speaks of finding islands of the cortical substance in the medulla and vice versa. Also of the medullary substance extending from the central vein to the capsule and the cortex from the capsule to the central vein.

Frequency.—Without endeavoring to make the search exhaustive, I have found references in the literature to 160 cases of hypernephroma, recorded since 1890; to these the present series of three should be added. Nearly or quite a dozen known unreported cases are not included in this list. Albarran and Imbert give the number of tumors of the kidney reported from 1890 to 1902 as 588; of these, 529 were subjected to histologic examination, and 90, or 17%, shown to be hypernephromas. In addition to those called hypernephroma, many tumors of the adrenal are reported as sarcoma or carcinoma, with the statement that they correspond partially or entirely to the description by other writers of hypernephroma. Rolleston,³⁴ in mentioning 26 cases of primary tumor of the adrenal, says that nine may be called either malignant adenoma or carcinoma, the former being closely allied to hypernephroma. Amberg³⁵ reports a primary malignant tumor of both adrenal glands in a child of two months, with secondary involvement of the liver. Though both primary and secondary growths reproduced the medulla of the adrenal, Amberg considers the tumor impossible of classification on such basis, because the histogenesis of the adrenal is not definitely decided. He therefore says it may be morphologically classed as either a carcinoma or an alveolar sarcoma. From his description it would appear that this tumor might, with propriety, be called a hypernephroma. Amberg refers to Pepper's³⁶ six cases as being similar, and gives a lengthy discussion of primary tumors of the adrenal. Woolley³⁷ discusses at length adrenal tumors. He speaks of "malignant" adenomas, but does not mention hypernephroma or even aberrant adrenals. From these statements will be seen the difficulty of determining the exact number of cases of hypernephroma, and the reason why no attempt has been made in this paper so to do. I am fully convinced the number cited is far too small, but cases reported as adenoma, carcinoma, or sarcoma, must be accepted as such, even though their metastases produce what seems to be adrenal tissue. That any attempt to number the cases must result in only an approximation, is recognized by Albarran and Imbert, who furnish elaborate tables of statistics regarding different tumors of the kidney, as to their frequency, symptoms, malignancy, etc., and then say there are so many bases of diagnosis that their figures are given only as curiosities.

Site.—Of the 163 cases of hypernephroma included in

this paper, 157 were in the kidney, 8 in the adrenal, 2 in the liver, and 1 in the uterus. This great preponderance of cases in one organ explains why the term, "hypernephroma of the kidney," is almost invariably used in reference to this tumor. As previously stated, it appears as if the number in the adrenal might be greatly increased were it not for the tendency among observers to avoid this term for tumors of the adrenals themselves. Clinically, the problem would be simplified, and but little change in the classification made necessary, if the name hypernephroma was restricted by all pathologists to primary tumors, and their metastases, originating in aberrant adrenal tissue only, and not to those springing from the normally placed organ. Still better, in the opinion of the writer, would be the application of the term "adrenal tumor" to all new-growths producing adrenal tissue, regardless of situation. Clinically, of course, they would be benign or malignant.

Morbid Anatomy.—In the kidney, hypernephromas are usually single, but not rarely multiple, and have been found in both organs. Regarding the side, they occur indiscriminately. Of the cases in this series in which it is specified, the tumor was in the left kidney 57 times, in the right 55. As to sex, 71 were in males, 45 in females. The tumors are situated beneath the capsule of the kidney and vary in size from a pin-head to that of a pea, in what may be called the strictly benign growths, and from this to the size of a child's head in the frankly malignant cases. When small they are almost always confined to the renal cortex, though they may be in the medulla. When large they project from the surface of the organ and also extend inward at the expense of renal structure until they reach the pelvis, which may be obliterated by pressure, but is seldom actually penetrated. Either pole or the middle of the kidney may be involved. In the former case one extremity, and in the latter both, may retain the renal outline and structure. The external surface of the tumor is lobulated by depressed bands of the capsule. The color is usually grayish-red or yellow, the latter predominating, but often there are brown or bluish, or even black areas, due to the presence in the tumors of small or massive hemorrhages. The tumor may be firm, but in many of the larger growths the projecting masses are softened, in some instances being almost cyst-like in consistency. Incision of the tumor reveals surfaces corresponding closely to the external appearance in color and in lobula-

tion. Masses within alveoli formed by the fibrous stroma may be so soft as to project, and even detach themselves from the surrounding tissue. The tumor is generally sharply outlined from any remaining renal structure by a distinct band of firm fibrous tissue. Hemorrhages into the tumors are exceedingly common and areas of softening, due to degenerative changes, are also frequently present.

Targett³⁸ found in one of his cases, on the lower and outer surface of the kidney, a yellowish body the size and shape of a finger-nail. The capsule was split and through the lower part the adrenal tissue extended into the kidney. Conversely a few convoluted tubules passed into the adrenal structure. His second case was one of a tumor two inches in diameter. Thorndike and Cunningham⁹ report three cases. They say the outline of the tumor is usually that of the kidney. It is commonly either encapsulated within the kidney or is situated immediately beneath the renal capsule. Eurich³⁹ found congenital atrophy of the kidney, the upper pole of which was two inches from the adrenal. The intervening space was occupied by a spheric tumor one inch in diameter, purple in color and encapsulated; on the upper pole was the normal adrenal. The histology of the tumor was that of the adrenal medulla, and Eurich believes the tumor originated in the adrenal gland. Plummer⁷ reports the case of a man of 68, who had a hypernephroma of one kidney eight inches in length; connected with it were three cysts, each containing two ounces of fluid. Boyd and McFarland⁴⁰ report a case appearing to follow pregnancy in a negress of 30; autopsy showed collapse of the tumor, the larger part of which had become necrotic. Between the tumor and kidney was fibrous tissue belonging to the tumor and also additional connective tissue, resulting from atrophy of the parenchyma of the kidney. Bevan⁴¹ reports a case in which the tumor projected into the pelvis of the kidney like a polypus. Two weeks after operation the patient suffered an attack of diarrhea and pieces of hypernephroma were found in the feces. Bevan has seen seven or eight cases, and considers hypernephroma the most frequent malignant tumor of the kidney.

Caird⁴² speaks of an enormous adrenal tumor that had engulfed the whole of a kidney. Brown⁴³ reports a large tumor of the right side, lobulated like the fetal kidney, and almost entirely composed of adrenal tissue. He also mentions three cases observed by other surgeons. Brown says certain facts regarding his case afford

reasons for the query as to the possibility of a kidney being so entirely made up of adrenal tissue, even at a time when it is not appreciably enlarged, as to be essentially functionless as an excretory organ. Of interest in this connection is the statement of von Frisch " that the cryoscopic point of the urine from a kidney in which a hypernephroma had caused the disappearance of the pyramids, was normal, thus leading to the supposition that the kidney was functionally perfect.

Morris (*loc. cit.*) says the relation, or apparent relation, of the capsule to the various tumors in and around the kidney is not reliable as a guide to their morbid anatomy. "The isolation from the renal parenchyma of a tumor situated immediately beneath the renal capsule is far from being decisive in favor of the theory of Grawitz; neither is the argument that the capsule of the kidney seems to be continuous over the tumor a decisive proof that the tumor originated in the kidney and not outside of it." A primary tumor of the adrenal may stretch part of the kidney over it as a hood. There is equal reason to believe that as a primary tumor grows downward it may invade and cause destruction of the kidney tissue. Morris⁸ later reports two primary tumors of the adrenal involving the kidney.

Thompson,⁴⁵ in speaking of liver abscess, says: "In disease of other organs I have only once met pus simulating that found in liver abscess. The case eventually proved to be a hypernephroma occupying the upper end of the right kidney. The symptoms simulated those of hepatic abscess, and an aspirating needle was thrust through the tenth intercostal space in the midaxillary line. At a depth of about two inches chocolate-colored fluid exactly like liver pus was withdrawn. It contained a few white flakes. No amebas were found. Operation revealed a normal liver and an enlarged kidney, the upper end being occupied by a cyst as large as a small orange. This was drained. A small piece removed from the wall showed the mass to be a hypernephroma." Harris⁴⁶ says when these tumors originate in the adrenal proper they are commonly separated from the kidney by connective tissue, and however much the kidney may be attached to or flattened by the growth, the latter may usually be separated and removed, saving the kidney to the patient. Bean⁴⁷ reports the removal of a tumor supposed to be a cystic kidney. Examination revealed a hypernephroma 15 cm. by 16 cm. (5 $\frac{1}{4}$ in. by 6 $\frac{1}{4}$ in.) in size. A. P. Ohlmacher⁴⁸ reports two cases of hypernephroma of the kidney. One was as large as

a child's head, removed by operation, with recovery of the patient; the other the size of a hickory nut, found at autopsy. Karewski⁴⁹ reports a case of multiple hypernephroma of the kidney in which suppuration had occurred. The appearance of the gross specimen was that of typical tuberculosis with multiple cavities. He knows of no other case of suppurating hypernephroma, and accounts for the complication in this instance by the general condition of the patient, who, although only 27, had had cholera, pneumonia, purulent pleurisy, appendicitis with abscess (opened), and cholelithiasis (operated). Chandler⁵⁰ observed a case in which the entire kidney, with the exception of the capsule, was replaced by adrenal tissue, measuring 24 cm. by 13 cm. by 11 cm. (9½ in. by 5½ in. by 4½ in.). Rupperecht⁵¹ found a hypernephroma of the right kidney in a child of 2½ years. There was no recurrence one year after removal.

When occurring in the liver, primary hypernephroma presents much the same appearance as those situated in the kidney. That reported by Vecchi⁵² was in the right lobe above the adrenal impression, definitely circumscribed and stated to be the size of a nut, from which we can infer but little as to the dimensions. It was intensely yellow, glistening, and distinctly lobulated by white bands, which, surrounding and penetrating it, caused bulging of the tissues between. Noyes⁵³ found a large tumor of the liver nearly identical with the structure of the adrenal and attributes its origin to an aberrant gland. There was no primary growth in the adrenals. To these two cases, three more might possibly be added, but I consider them better placed under the head of ectopic adrenals.

But one case of hypernephroma of the uterus appears to be on record. This was exhibited by Eastwood⁵⁴ and was a large malignant growth attached to the fundus, being separated from the uterine tissue by a fibrous capsule. The zona glomerulosa of the adrenal was represented, the tumor showing typically the features of a malignant adrenal growth. Eastwood also showed two such tumors in connection with kidneys.

Metastases.—A most interesting part of the morbid anatomy of hypernephromas is the occurrence of metastases. This at once raises the question of the clinical character of this group of tumors. From the descriptions already given it readily may be seen that the small hypernephromas giving rise to no symptoms and found only at autopsy are as benign as the adrenal rests from which they spring. It is just as evident that the

larger growths, which extensively destroy surrounding tissues by pressure or by actually breaking through the capsule, possess malignant attributes. This attains its highest degree in the formation of metastatic growths in other tissues of the body. These varying clinical manifestations of hypernephroma not inaptly have been compared to true adenomas of other tissues which later develop malignant characters. On this basis, all hypernephromas may be regarded as potentially malignant. Eisendrath³⁸ says the so-called Grawitz tumors are an intermediate class between benign and malignant groups, occurring in the circumscribed form as benign, or in a more diffuse manner as malignant growths. Neusser (loc. cit.) calls attention to the fact that apparently benign hypernephromas are capable of giving rise to metastases larger than the primary growth. Metastases are most frequently found in the lungs, the liver, and in bones, but almost all other tissues of the body have been invaded. The discussion of this phase of the subject will, we believe, prove of most interest and value if the various points are taken up in connection with the exceedingly instructive series of reported cases.

Schultze³⁹ obtained postmortem specimens including several organs. There was a tumor of the left adrenal, the organ being four times its normal size. The right kidney was eight times as large as normal, nearly all tumor; this growth extended through the renal vein into the vena cava as far as the liver. There were a number of isolated metastases in the visceral layer of the pleura, about the bronchi, and in the left kidney. The lower epiphysis and adjoining shaft of the right femur was invaded and increased four times in size; absorption was marked, the bone being easily fractured and even cut through by a knife. In the discussion, Brooks said he had seen two cases, one of which showed metastases in the corpora cavernosa. Kelly (loc. cit.) reports four cases of hypernephroma of the kidney and one of the adrenal, four of which gave rise to metastases and the fifth invaded the renal vein and ureter. The tissues involved in the secondary growths were the peritoneum, vesical plexus and mucous membrane, vena cava, and lungs.

Bierring and Albert⁴ report five cases of hypernephroma of the kidney, three of which (collectively) produced metastases in the liver, lungs, intestine, and retroperitoneal lymph-nodes. They discuss at length the method of metastasis, which they believe occurs most frequently through the blood by way of the renal vein.

That extension through the lymphatics does occur, though rarely, they consider proved by their case with involvement of the retroperitoneal lymph-nodes and also by the case of LeCount which included invasion of the lymph-nodes in the left inguinal region. They believe involvement of the liver by secondary growths is due in most cases to retrograde embolism through the vena cava and hepatic vein. In the discussion of this paper McCallum, of Baltimore, said a number of cases of hypernephroma occurring at the Johns Hopkins Hospital indicated that the most frequent metastasis was by way of the blood-vessels. He does not, however regard the secondary growths in the liver as best explained by retrograde embolism. In one case the liver was almost filled by nodules and it is difficult to believe they could have come from the vena cava directly. He believes the tumor cells passed through the lungs, although none appeared to lodge in those organs. Coplin suggested the possibility of hepatic metastases through the portal circulation rather than the lungs, aberrant vessels from the adrenal structure furnishing the mode of entrance to that system. A. P. Ohlmacher (*loc. cit.*) reports a case occurring in the service of Van Hook in which the tumor and kidney weighed 4,725 gm. The vena cava contained a thrombus extending through the diaphragm and also into both iliac veins. The liver was filled with metastatic nodules which Ohlmacher attributes to retrograde embolism. Brown (*loc. cit.*) showed three specimens obtained by colleagues. One patient died three years after operation, from metastases (location not given). In the discussion of this paper, Lilienthal said he had seen three cases. One man died from prompt recurrence and a woman operated on one year ago has a probable metastasis in the frontal bone. Hardou,⁵⁷ in reporting a case in which the right kidney was the site of a tumor, says that when hypernephromas are malignant it is to a less degree than are sarcomas.

Clairmont⁵ found an egg-sized hypernephroma in the lymph-nodes at the bifurcation of the trachea. The patient had been operated on 10 years previously for a tumor of the right kidney. At that time the right pleura was opened and, it is believed, infected by tumor cells, which were carried by the lymph stream and deposited in the nodes. The tumor in the mediastinum had grown slowly under unfavorable circumstances. Holmes (*loc. cit.*) found in a subject, who had a tumor of the left kidney (or adrenal), the right lung filled with

solid tumor masses and also three small foci in the left lung. Böhler⁵⁵ discusses 37 cases, 10 of which are original. Of these 13 had metastases, 12 in the lungs. The other sites of the metastases were the opposite kidney, pleura, retroperitoneal lymph-nodes, femoral vein, adrenal, femur, inferior vena cava, liver, dorsal vertebrae, ribs, temporal lobe and frontal sinus, and the wall of the left ventricle of the heart. J. C. Ohlmacher⁵⁶ reports the case of a woman of 49 from whose left kidney was removed a hypernephroma the size of an orange. She died in six weeks from metastases in the left temporal bone, right side of neck, left breast and axilla, right abdominal wall, and beneath the line of incision in the lumbar region. The renal vein was invaded. This tumor reproduced the medulla of the adrenal. Jellinek⁶⁰ reports two cases. In one a tumor of the right kidney was firmly attached to the under surface of the liver and sent a cone-shaped projection into the inferior vena cava. LeCount⁶¹ found in the right kidney of a subject one hypernephroma the size of a hen's egg and several smaller ones. A retroperitoneal growth extended into the bony pelvis and through the first sacral vertebra, producing a tumor of the buttock with ulceration and gangrene. Metastatic growths were found in the left femur and left iliac lymph-nodes and pathologic fractures of the right ilium and left femur had occurred.

Histology.—As the microscopic characters of the tumors reported in this paper have been described with some detail, and are fairly representative, more than brief reference to certain general features of the histology of hypernephroma is not at this point demanded. The tumors reproduce more or less perfectly the structure of the adrenal gland, usually one or more layers of the cortex, rarely the medulla, being represented. They possess a fibrous capsule, but this may be penetrated and even partially destroyed by rapidly growing tumors. The two prominent features are the stroma and the cells. The former may be composed of quite dense bands of fibrous tissue, but commonly consists of capillaries with walls of endothelial cells only. In the larger growths, both types are frequently represented, vascular fibrous bands dividing the tumor into large lobules or alveoli which in turn contain a capillary network. The relatively large cells of the tumor are round, polygonal, or even columnar in type; usually they rest on the stroma or the endothelium of the capillaries, but often become detached and lie free in the larger spaces. The cytoplasm is scanty and granular and contains numerous

vacuoles marking the former site of dissolved fat. The nucleus stains deeply and a nucleolus is generally conspicuous. By some, considerable diagnostic value is placed upon the fact that the nucleus and nucleolus stain dissimilarly. Glycogen can usually be demonstrated in these cells. Giant cells not infrequently occur. Kelly ascribes diagnostic importance to the presence of granules of intensely black pigment similar to those normally present in the adrenal cortex. He believes the cysts found in some hypernephromas originate in renal tubules enclosed within the adrenal tissue, and this point has been substantiated by other observers. In all tumors of any considerable size, degenerative changes are a prominent feature. Hemorrhages are often conspicuous, and are largely responsible for the marked color variations seen in many of the tumors.

Pathologic Physiology and Chemistry.—The question of increased arterial tension as a manifestation of hypernephroma may not improperly be considered at this point. This implies hypersecretion by adrenal tissue or the excessive introduction of its secretion into the circulation, and applies more properly to tumors of the adrenal gland itself, but has been observed in cases of hypernephroma of the kidney. Certain writers strongly emphasize this point; the majority entirely disregard it. Ochsner⁶² states that the tumors of Grawitz cause severe systemic disturbance, the principal symptom being greatly increased arterial pressure. "The patient rapidly becomes sick and dies, usually with a hemorrhage into the brain or other important structure." Sippy (*ibid.*) said he knows of only four reported cases in which adrenal tumor of the kidney was accompanied by greatly increased arterial tension. Two cases, seen post-mortem in Vienna, which were accompanied by cerebral hemorrhage sufficient to cause death, had high arterial tension during life. He states that Neisser and Holmes each report a similar case, but gives no reference to their papers. Sippy does not consider increased arterial tension a diagnostic sign of much value. An editorial writer⁶³ mentions two cases of high arterial tension accompanying hypernephroma. One patient suffered from persistent headache until the tumor was removed. The second was supposed to have renal sclerosis, the pulse being always of high tension, though the patient was pale. This writer says the size of the tumor does not determine the virulence of the intoxication. A small tumor may cause cerebral hemorrhage, or a large one may give rise to no marked circulatory symptoms.

Vaquez⁶⁴ reports an adenoma of the adrenal removed at autopsy; the patient had had a persistently high arterial tension. The occurrence of secondary softening of the brain in Case III of our series is exceedingly suggestive, even though the associated arterio-sclerosis in itself might easily account for cerebral hemorrhage. Neusser (*loc. cit.*) suggests the possible diagnostic value of injecting into animals the urine of patients supposed to possess an adrenal tumor, to determine if it cause increased blood-pressure. Cooper⁶⁵ says the technic necessary for this is too complicated for general use, and recommends injecting the urine into the ear of a rabbit and noting if changes occur in the easily observed vessels of that organ. The whole question of increased arterial tension in hypernephroma can be considered as entirely unsettled, clinical observation on this point having been sadly neglected. This is readily explained by the fact that the tumor is seldom diagnosed before operation. The point is one that should be investigated, however, in every case of suspected adrenal or renal tumor.

The diagnosis of gross specimens of hypernephroma by the iodine-starch reaction of Croftan⁶⁶ deserves mention. Several observers attest its value, but at present I cannot similarly endorse it. The reaction was obtained with a part of the tumor in Case II, after it had been for several months in formalin. An obscure tumor of the liver, thought possibly to be a hypernephroma, also gave the reaction. Testing its value further, we obtained a positive result with a tuberculous mamma, fresh, and a formalin-preserved mixed tumor of the parotid gland. Further experiments will be necessary to convince us of the specificity of the reaction of this test.

Since the demonstration that a part of the fat content of the cells, particularly the spongiocytes, of the adrenal gland is lecithin, the search for this substance in hypernephromas, as a diagnostic aid, has been suggested. The difficulty of isolating this substance rendered the question for some time of academic importance only, but Bernard, Bigart, and Labbe⁶⁷ appear, in part at least, to have solved that problem. The diagnostic value of lecithin in tumors, however, remains to be determined. Albarran and Imbert do not consider it, any more than fat or glycogen, pathognomonic of hypernephroma.

The privilege of studying two of the present cases I owe to Dr. Keen; the third to Dr. W. M. L. Coplin. I am deeply indebted to both for their kindly interest and assistance in the preparation of this paper.

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A STUDY OF HOMOGENIZED CULTURES OF TUBERCLE BACILLI.

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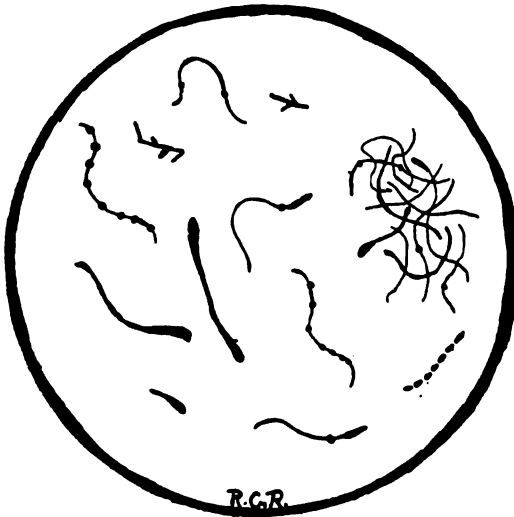
The growth of human, bovine, piscum, or avian tubercle bacilli in bouillon, has a tendency to form a scum or pellicle, in the absence of which, under ordinary conditions, no growth is obtained. This pellicle may be started by floating a small mass of the transplanted culture upon pieces of cork (Coplin), or by using sterile oil for the float. This floating can be accomplished without either cork or oil, if great care is exercised not to wet the whole mass. To obtain what is called a homogenized culture, quite different technic is employed.

The first to call attention to this special cultivation of the tubercle bacillus was Ferran,¹ who recommended inoculating into a succession of bouillons successively poorer and poorer in sugar and glycerin.

Arloing² recommends for the preparation of cultures for the agglutination test, potatoes, which are placed in a tube containing a small quantity of a 6% solution of glycerin, just enough to touch the lower end of the potato. After inoculation, the tubes are kept in the incubator at 38° C. to 39° C. On every second day the tubes are tipped, so that by the inclination of the tube the glycerin solution is caused to flow over the culture on the surface of the medium. Under these conditions, growth occurs rapidly, the resulting masses of bacilli differing from those in ordinary cultures, in that they are soft in consistency, and easily broken up by a glass rod or by rubbing in a mortar. From these cultures, subcultures are made in veal broth, and submitted to daily shakings to keep the organisms separate one from another; but even in these preparations, it is impossible to prevent some clump formation. The majority of the organisms are isolated, the fluid is turbid, with but little sediment. According to Courmont and Descos, the

more numerous the transplantations, the better the resulting homogeneity. When the pseudotubercle bacilli are experimented with, a scum is likely to form in a few hours, so that repeated shakings are absolutely necessary. With the bacillus of human tuberculosis, as the film does not form until several days of repose, there is less trouble in obtaining homogeneous cultures.

Hawthorn³ recommends growing the tubercle bacillus in a medium consisting of peptone (Defresne) 20 gm., sea salt 7 gm., water 1 liter; neutral to litmus, but faintly acid to phenolphthalein.



Aberrant forms of the human tubercle bacillus from a culture three months old. (Homogenized preparation.)

Auclair⁴ gives the following technic for obtaining a homogeneous and at the same time a saprophytic form of the tubercle bacillus. The organism is sown on a beef bouillon containing potato, salt, sugar, and glycerin. At the end of 20 days it will be found that the previously clear medium has become slightly cloudy, without the formation of a pellicle, but later with a tendency toward the development of a deposit.

My experiments in obtaining homogeneous cultures of tubercle bacilli were made by using glycerin-agar and glycerin potato growths, and inoculating into a 5%

glycerin bouillon. The agar preparations were made originally from a homogenized bouillon culture. The method of inoculating the bouillon consisted in taking upon a platinum wire loop a small portion of the growth from potato and rubbing it thoroughly upon the side of the tube or flask. The bouillon was brought in contact with the growth by rotating the receptacle, thus washing off and at the same time disseminating the organisms throughout the medium. The culture was placed in the incubator at 37° C., and several times a day the flask was shaken to prevent the bacteria precipitating or forming a pellicle. The growth of the human tubercle bacillus was noticed as early as the third or fourth day, when turbidity of the medium was apparent. The cloudiness persisted and increased, and resembled vigorous cultures of *B. typhosus*. If the flask was not shaken a very granular and amorphous sediment formed. In all these cultures, in addition to the sediment, pellicle formation took place, and when this was shaken down another formed in a couple of days. In one preparation a third pellicle developed, though it was more scanty and delicate than the two previous ones. When glycerin agar was inoculated from a bouillon culture, growth was usually observed within five to seven days, the fully formed preparation was moist or creamy in appearance and consistency, and could be easily removed and readily spread upon other culture mediums. A perfectly homogenized preparation will remain turbid indefinitely, but eventually a sediment forms or a pellicle appears. I was also successful in obtaining a perfectly homogenized preparation of the human tubercle bacillus in plain bouillon at the temperature of the body and at ordinary room temperature. In the incubator, at body temperature, growth was abundant, and appeared as early as the fifth day, while at ordinary room temperature only slight turbidity was noticeable at the end of two weeks. The method of inoculation was the same as mentioned for the ordinary homogenized preparations. The appearance of cultures in plain bouillon was exactly like those in glycerin bouillon.

In homogeneous cultures of the human tubercle bacillus the morphology and microchemic reactions are but little different from growths upon blood-serum or upon glycerin-agar.

Auclair claims that the homogeneous tubercle bacillus is a strict aerobe; the elements longer and larger than the ordinary bacterium and actively motile. Hawthorn

states that the motility of tubercle bacilli upon his special medium is most striking, and notes the presence of free spore-like bodies. Arloing maintains that the homogenized tubercle bacilli are motile, and from his description of these motile forms of the organism, Koch doubted the identity with his own bacillus. Loeb⁶ denies motility though the usual brownian movement is present. I was unable to demonstrate motility in any of the cultures examined, even in cultures only four or five days old. Brownian movement was evident in nearly all preparations. Marmorek asserts that homogeneous cultures, when young, lose their virulence, and in part their resistance to acids. In my experiments young homogenized bacilli resisted 25% solution of sulfuric acid just as markedly as preparations from an agar culture. In morphology the human tubercle bacillus was very pleomorphous, exhibiting short and long forms; some of the former were so small that they were almost coccoid, while the latter were filamentous in nature. Beaded forms were common, club-shaped bacilli and branched organisms were occasionally encountered. In cultures three months old, the individual elements were very long, 10 microns to 12 microns being an average size. Some were thin, others thick; some stained darkly, the remainder stained very faintly. Quite a few contained small, deeply-stained granules, which slightly exceeded the diameter of the organism itself. As many as eight of these granules were observed in a single element. This filamentous character was quite constant, the threads resembling closely those seen in streptothrices. Large, thick, irregularly staining or beaded forms were common in old cultures. Although the greater number of the organisms were isolated and ungrouped, there was a decided tendency to collect in small masses of from 6 to 12 or 15 elements. Five cubic centimeters of the homogenized bouillon culture inoculated into the peritoneal cavity of a guineapig, produced caseous nodules ranging in size from 5 mm. to 2 cm. Spreads made from these lesions contained numerous beaded, long, acid-fast bacilli.

Homogenized cultures were also made of *Bacillus tuberculosis piscum*, *Bacillus tuberculosis avian* as well as of Moeller's grass bacillus.

B. tuberculosis piscum.—The individual elements were pleomorphous. Small coccoid forms were abundant in young preparations, while suggestively filamentous forms were present in older cultures. The average

length of the organisms was about two microns. Beading was also noticed, and in this form the bacterium stained less darkly than the other solidly staining elements. No clubbed bacilli were present, and although pairs were frequently observed, isolated bacteria predominated; the tendency to form in groups was not especially noticeable. They were amotile, although an active brownian movement was apparent. Resistance to 25% solution of sulfuric acid was still retained in old cultures, though to a certain extent lost in very young growths.

B. tuberculosis avian.—Like the previous organisms, this bacterium was also pleomorphous. Very small almost coccoid forms were present; others were from 5 microns to 6 microns in length. The long forms showed a decided tendency to club formation, while a smaller, thin variety appeared as if fractured near the center, causing it to resemble a diplobacillus. Beaded bacilli but no filaments were present in young cultures, though the latter form was abundant in preparations six months' old. The tendency to form in groups was decided, although individual bacilli were present in every field. There was not the slightest brownian movement or motility of any kind noticeable in young or old cultures. Resistance to 25% solution of sulfuric acid was well preserved.

Moeller's Grass Bacillus, No. II.—This organism was taken as the type of the pseudotubercle bacilli. The individual elements in cultures two weeks old were short, stout, and oval; very few, if any, long forms, and no beaded or clubbed forms, were seen. Some bacilli were decolorized by 25% solution of sulfuric acid, while the greater number still resisted the reagent. An agar culture made from the homogenized preparation was of the color and consistency of cream. Spreads made from this growth contained many long and beaded forms, which were quite resistant to 25% solution of sulfuric acid.

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ON THE PATHOGENESIS OF LEAD INTOXICATION APROPÓS OF THE PATHOLOGIC FINDINGS IN A CASE.*

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The present report is a contribution to the question of the effect of lead on the nervous system. While it does not elucidate completely the pathogenesis of the disease, it nevertheless shows the inadequacy of the views of those who adhere persistently to one certain theory. Lead carries its deleterious effect not to one special element of the nervous tissue, but to all its constituents simultaneously; the difference may lie in the degree, but not in the localization.

C. A., male, aged 48, a leadworker by occupation, was admitted to the Philadelphia Hospital in June, 1903, with double wrist-drop, and history of colic. After a course of treatment, lasting four weeks, he was discharged, practically cured. In December of the same year he began again to lose power in both arms. He was readmitted to the hospital January 7, complaining of severe pain in the abdomen, chest, back, and legs, of frequent micturition, and of loss of power in the upper extremities.

Examination shows an emaciated and cachectic-looking individual. The eyes have a yellow-tinged conjunctiva. Pupils react to light and accommodation. Tongue is heavily coated, and a blue line at the margin of gums is distinct. The peripheral arteries show arteriosclerosis. There is a total brachial palsy on both sides. A test for each individual muscle shows complete loss of power, except both triceps muscles, which are preserved to some extent. Musculature of shoulder girdle, including the muscles of the scapula are flabby; the latter are distinctly atrophied. Grip in both hands is markedly reduced, and the wrist-drop is double. Tendon reflexes in left arm are entirely abolished, but only diminished in the right. Bechterew's reflex is abolished on the left side, and very much diminished on the right. The knee-jerks are normal; there is no foot-drop on either side. No Babinski, no ankle-clonus. There are

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no objective sensory disturbances in the upper and lower extremities. The nerve trunks are not painful on pressure, but patient complains of pain in the right upper limb.

As death occurred on the third day after admission, no detailed examination could be made.

Autopsy showed a vesicular emphysema of both lungs, fibroid myocarditis, simple atrophy of the heart, chronic interstitial nephritis, chronic cystitis, and atheroma of the aorta and large vessels. The pia arachnoid of the brain was edematous; the cerebrospinal fluid was quite abundant. No gross lesion was noticed on the brain or spinal cord.

The spinal cord and pieces of the following nerves of both sides were kept for microscopic study: Musculospiral, median, ulnar, and sciatic. The brain, unfortunately, was given in a condition unfit for examination.

Left Ulnar Nerve (Weigert).—Degeneration is slight, but distinct. Out of five or six nerve bundles only one shows degenerated fibers. The latter bundle is in the vicinity of a very large and dilated bloodvessel. The small nervi nervorum situated at the periphery show some degeneration. There is no thickening in the perineurium, endoneurium, or epineurium. The bloodvessels in the epineurium show thickening, especially of the intima, so that their lumen is almost entirely occluded. No recent degeneration could be seen with Marchi.

Right Ulnar.—Some degeneration of the same character as on previous section, which is better seen with Marchi stain, but there is no recent degeneration. The bloodvessels are very thickened and enlarged.

Left Median.—Degeneration is more pronounced than in the ulnar nerve; the walls of the bloodvessels are decidedly thickened, even within the individual bundles. There is perhaps a slight thickening of the epineurium. No recent degeneration is seen with Marchi.

Right Median.—Some degeneration in the bundles, also in the nervi nervorum. Bloodvessel changes are also very slight. There is a distinct increase in the connective tissue surrounding the nerve bundles. No recent degeneration with Marchi.

Right Musculospiral Nerve.—A certain amount of degeneration in many bundles. Bloodvessel changes are distinct. No recent degeneration with Marchi.

Left Musculospiral Nerve.—Degeneration is somewhat more marked than in previous sections, but the vessel changes are *unusually* marked, dilated, deformed, thickened. Some recent degeneration is noticed in this nerve.

Left Sciatic Nerve.—Distinct vessel changes. A few scattered, slightly degenerated, bundles; degeneration is more marked in nervi nervorum. No recent degeneration with Marchi.

Right Sciatic Nerve.—Scattered slight degeneration in nervi nervorum. Vessel changes marked.

Cord.—Fourth cervical segment: No degeneration of tracts or roots is seen with Weigert. Bloodvessels show thickening of the walls, particularly those which are in the vicinity of the anterior and posterior roots. Marchi's stain shows no recent degeneration. Fifth cervical: Marchi. No degeneration is seen in the cord itself, but the anterior and posterior roots are covered with black droplets, not abundant, but still distinct. Sixth cervical: Weigert shows only some slight degeneration of the anterior roots, none in the posterior. Bloodvessels present marked changes, but of the same nature as above. No recent changes are seen with Marchi. Seventh cer-

vical: Weigert shows some degeneration in anterior and posterior roots (in the latter more than in the former). In the posterior columns near the middle line adjacent to the septum and at equal distance from the posterior commissure and the periphery a light area imperfectly stained is seen and contrasts strikingly with the neighboring portions which are deeply stained. Bloodvessel changes not marked, but distinct. Marchi shows some droplets in the anterior roots, but not in the posterior. In the previously-described light area of the posterior columns are seen black droplets when stained by Marchi.

Thoracic.—Traces of degeneration are found in some bundles of the anterior roots; vessel changes are very marked. Marchi negative.

Lumbar.—Distinct degeneration in the posterior portions of the posterior columns, more marked on one side than on the other. The posterior roots also show distinct involvement in their extramedullary and intramedullary portions, more on one side than on the other. Some bundles of the posterior roots are slightly degenerated. The periphery of the anterior columns as well as the neighboring portions of the anterior roots are distinctly degenerated. Marchi's stain shows recent degeneration in the posterior roots, but none in the anterior. The vessel changes are the same as in the other section. The posterior roots show very marked loss of axis cylinders, while in the anterior this is only slightly noticed.

Cells.—While many cells are apparently normal, there are nevertheless quite a number showing deformities, nuclear displacement, pigment degeneration and chromatolysis. Changes are more marked in the cervical region than in the lumbar.

Meninges are moderately thickened, no leukocytic infiltration can be seen. Staining for axis cylinders shows a very marked destruction in the left musculospiral nerve, and very slight destruction in the right musculospiral nerve. In the right median nerve only a small number of axis cylinders are missing, while in the left median they are all preserved. Quite a large number of destroyed axis cylinders were found in the left ulnar nerve. In the sciatic nerves they are normal. As to the cord, in the cervical segment the anterior roots show more destruction of axis-cylinders than the posterior. In the lumbar cord the posterior roots and posterior columns show a very marked loss of axis cylinders, also to a great extent the anterior roots and anterior columns.

A brief review of the findings shows that degeneration is found in all the nerves examined, but in a moderate degree very few bundles are affected. Exception may be made for the musculospiral nerves. In the latter are found more degenerated portions than in any other nerve; this difference, however, is only quantitative, not qualitative. The same cannot be said about the bloodvessels; the changes of the latter, although markedly present in all the nerves, are unusually pronounced in the left musculospiral nerve. Marchi's method shows no trace of recent degeneration. Connective-tissue changes are detected only in the median nerves, in the left more than in the right.

The spinal cord presents some interesting changes. No changes in the tracts or roots are noticed in the upper cervical segments, but in the lower portions some degeneration is seen in the columns of Goll, in the anterior roots—with the Weigert and Marchi; although the degeneration is slight, it is nevertheless distinct. The thoracic cord shows some degeneration in the anterior roots only with Weigert's method. The lumbar cord presents the most interesting findings; Weigert's stain shows distinct degeneration not only in the posterior and anterior roots in their extramedullary and intramedullary portions, more on one side than on the other, but also (a fact which is quite unusual) in the posterior portions of the posterior columns, and in the very anterior portion of the anterior columns.

Repeated examination of a large number of sections showed distinctly a deep, dark staining of the white matter except the areas mentioned, which always appeared very light gray. Marchi's method showed recent degeneration in the posterior roots, but none in the anterior. The bloodvessels throughout the cord showed the thickening, dilation, and thrombi mentioned.

Among the nerve-cells of the anterior cornua we found some which present distinct changes (chromatolysis, nuclear displacement, etc.).

When we attempt with these pathologic findings before us to explain the clinical phenomena observed during the patient's life, we find a discrepancy at first glance. The changes in the cord are more marked in the lumbar region than in the thoracic and cervical segments, and still there was no paralysis in the lower extremities and the knee-jerks were preserved. At the level of the lower cervical cord the anterior roots are only slightly involved, and still the brachial palsy was almost complete, but if we take into consideration the conditions of the cells and of the peripheral nerves themselves, this apparent paradox can be somewhat explained. We said before that the cells in the lumbar region are only very slightly involved as compared with the lower cervical; also that the sciatic nerves show very slight changes. The absence of paralysis and the preservation of the patellar reflexes find therefore their explanation. The only obscure point, we find, concerns the changes in the posterior columns with intramedullary and extramedullary portions of the posterior roots. This case therefore proves that the knee-jerks do not entirely depend upon the condition of the posterior columns. In

the palsied condition of the upper extremities the most conspicuous phenomenon was the wrist-drop, which, as we know, is the clinical manifestation of an involvement of the musculospiral nerves. This corresponds to the pathologic findings of these nerves, which showed more degeneration than any other nerve.

Let us see if the pathologic changes in the cord and nerves of the present case will throw any light upon the question of the pathogenesis of lead-poisoning which, as is well known, is still debatable. All the experimental studies on animals show a remarkable uniformity of changes in the cells of the anterior cornua, but in man, cell changes were found by a comparatively lim-



Lumbar segment. Degeneration of the roots and posterior columns.

ited number of investigators (Vulpian, Oppenheim, Monakow, Oeller, Zannker, Goldflam, Stieglitz, Spiller.) The great majority failed to find cellular changes, but undoubtedly noticed changes in the peripheral nerves or roots. On the other hand, no changes whatever were found by some observers. How to reconcile the fact that in some cases the ganglionic cells were altered and in some not?

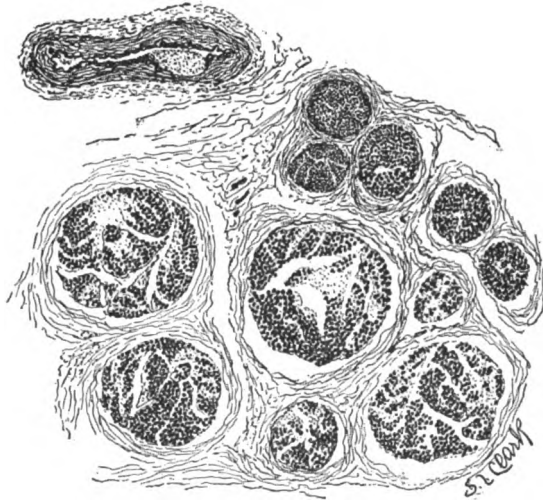
The clinical picture of the disease, the symmetric distribution of motor disturbances, met in every case, the want of parallelism between the seat of the disturbance and the course of the nerve trunks, finally the comparatively slight changes found in the nerve trunks,

while the clinical manifestations were pronounced, all these facts certainly argue in favor of a central origin of the disease; in those cases in which no cellular alterations were found, perhaps there was only a dynamic or circulatory disturbance sufficient to interfere with the functional activity of the cells, and thus produce the symptomatology of poliomyelitic palsies. The question whether a functional disturbance of the central end of a neuron (cell), is capable of being followed by a degeneration of its peripheral end, is still to be determined, but apparently it has its *raison d'être*. The central theory, therefore, explains the pathologic findings of the anterior roots and nerve trunks, but it is certainly incapable of accounting for the changes of the posterior roots, which were found affected in a certain number of cases. In such cases we must admit a peripheral origin of lead palsy. In other words, lead has no special predilection for special elements of the nervous tissue; while in some cases it affects primarily the cells, in others it involves the roots, and in still others the peripheral trunks, or all the three portions simultaneously. Perhaps the *locus minoris resistentiæ* is a potent factor in localizing the deleterious effect of the poison. It seems, therefore, to me, that this view is more in accord with clinical and anatomic data, and that neither of the two theories *per se* can be accepted.

In my case cellular changes were found in the cervical and lumbar segments, in the first more than in the second. The anterior roots were involved from the lower cervical segments down to the lowest lumbar portion. The posterior roots and partly the posterior columns showed some changes in the cervical and considerable in the lumbar cord. All the peripheral nerves showed some degeneration. It is true that all these changes were not pronounced, and sometimes even exceedingly slight, they were nevertheless undoubtedly present. A careful analysis of the foregoing findings shows with evidence that the condition of the cells alone will certainly not explain all the root changes throughout the cord or the nerve changes. The presence of posterior root and posterior column changes cannot be explained by the slight changes in the lumbar cells or by the slight changes in the sciatic nerves. In the latter case, if the peripheral theory is correct, the sciatic nerve changes must be pronounced, or at least more marked than the root changes, while in our case the condition is reversed. The mixed view mentioned should therefore be accepted;

the poison carries apparently its action simultaneously to all the elements of the neurons.

It remains to consider the vascular theory. That a deficient blood supply caused by vessel changes is apt to produce degeneration or destruction of nervous elements is easily conceived. In chronic lead intoxication, arteriosclerosis is almost a common finding. In our case the alteration of the bloodvessels was almost uniform through the entire cord and all the nerves. The most marked changes were found in the musculospiral nerves, especially on the left side, where the elastica is broken down and new fibrous formations are seen almost to



Left musculospiral nerve. Degeneration.

obliterate the lumen of the vessels; the arterioles in each nerve bundle between isolated nerve fibers are considerably thickened. Such changes are certainly sufficient to interfere with the function of the peripheral nerves, and still, in spite of the generalized arteriosclerosis, the paralysis was limited to the upper extremities. Consequently, it is reasonable to conclude that the vascular theory alone, similar to the cellular and peripheral, cannot explain the nervous phenomena of lead intoxication. However, there can be no doubt that it plays some role, as it is seen from the marked arterial

changes found in the musculospiral nerves, at which level the motor phenomena were the most pronounced. The so-called mixed theory mentioned should also include the influence of the altered vascular system.

In reporting this case I wish to call attention to the following points: 1. Involvement of the cells of anterior cornua. Comparatively few cases reported in the literature showed cellular changes. Although the diseased cells are not numerous, they are, however, present. 2. Very slight degeneration in all the nerves and roots. The paralysis of the upper extremities was nevertheless almost complete. 3. Involvement of the posterior roots and posterior columns in the lower cervical and in the lumbar cord. The involvement of tracts in the cord is an infrequent occurrence in lead intoxication. The majority of those cases in which cord changes were found presented degeneration of a disseminated character. There are however, a few cases on record showing systemic involvement. Pal, in his work on multiple neuritis in 1891, describes a case of chronic lead-poisoning which came to autopsy; polyneuritis of the peripheral nerves with extensive changes in the posterior roots and posterior columns was found. In E. D. Fisher's¹ observation the columns of Goll were sclerosed. E. Redlich's² case is one of chronic lead-poisoning associated with tabes and verified on autopsy. Carl Bechtold³ has reported recently a case of spastic paraplegia caused by lead-poisoning. The findings in my case are therefore of special interest from the standpoint of the pathogenesis of lead-poisoning. It shows that not one theory advanced can be accepted individually, but that several elements play their role in the causation of paralysis. With Vierordt, Raymond, and Perrier I think that lead exerts its deleterious influence upon the central tissue, peripheral nerves and bloodvessels simultaneously.

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¹ American Journal of Medical Science, 1892.

² Wiener medicinische Wochenschrift, 1897.

³ Münchener medicinische Wochenschrift, September, 1904.

CHORIOEPITHELIOMA MALIGNUM.

WITH REPORT OF A CASE.*

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PHILADELPHIA.

I recently secured, in the service of Professor Montgomery, in his gynecologic clinic in the Jefferson Medical College Hospital, a tumor of the uterus which is comparatively new, of decided pathologic and clinical interest and worthy of permanent record.

Patient.—R. M., female, white, married, aged 31.

Family History.—One brother died of pulmonary tuberculosis and one maternal aunt of cancer of the uterus.

History.—The patient suffered all the diseases of early childhood; otherwise she had comparatively good health. She menstruated first in her eighteenth year, and the periods were always regular and somewhat painful. She was married at 18 and has had five labors. The first four were normal, but the fifth occurred at the eighth month and was hastened or produced, she states, by sustaining a rather severe fall. The last child died in six weeks.

Present Illness.—This began about six months before the admission to the hospital and four months after delivery. There was more or less vague and indefinite pain, of a dull, aching, boring character, in the lower portion of the abdomen. She suffered constant and increasing distress in the back and head. Two months prior to admission she suffered from rather a free serous and offensive vaginal discharge. During the past six weeks the discharge has greatly increased in quantity and occasionally is mixed with blood. The bleeding is also progressively increasing. The patient is extremely pale and anemic and has lost, she says, considerable flesh. She complains of extreme weakness and is easily fatigued. The urine report is negative.

* From the laboratories of the Jefferson Medical College Hospital.

Examination.—On bimanual examination the cervix is found to be large and soft. The external os and the cervical canal are open and admit the tip of the index finger. The uterus is apparently $2\frac{1}{2}$ times its normal size, of about normal consistence and freely movable. The extrauterine tissues are palpably free from disease. A rather hard, circumscribed prominence was discovered in the right groin immediately below Poupart's ligament.

Operation.—May 19, 1904, Prof. E. E. Montgomery operated. The patient was prepared for combined operation, and before opening the abdomen the cervix was completely dilated and the interior of the uterus explored. A small amount of material was removed, and this so resembled malignant tissue that hysterectomy was decided on and was performed. The abdominal route was selected.

Pathology.—The uterus was $2\frac{1}{2}$ or 3 times its normal size and of normal consistence. The enlargement was general and

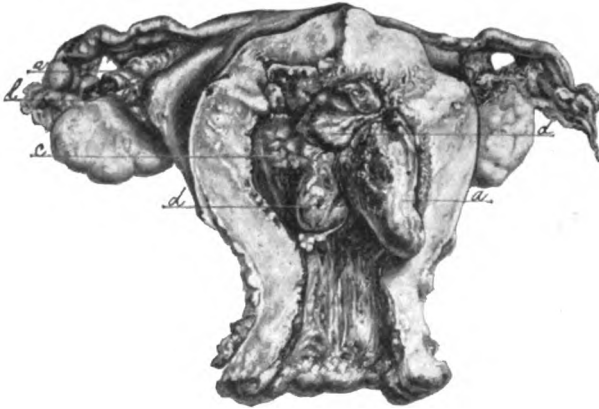


Fig. 1.—Drawing of gross specimen. a, Ovarian vein distended with organizing thrombus. Portion of thrombus protruding from the vessel. b, Round ligament. c, Tumor infiltrating mucosa and muscular wall. d, d, d, Three large nodules forming major portion of growth.

uniform, though nodulations could be defined in its interior. The uterine wall on incision was found to be thickened and showed the general changes found in chronic metritis. The tissue cut with normal resistance. On exposing the interior of the organ a large, irregular, nodular mass was found occupying the posterior and fundal wall. This was of a greenish "blood-coagula" color and of rather tense consistence. The nodules varied in size from a pea to a man's thumb and were spread completely over the posterior wall. The mass did not show any line of demarcation between itself and the uterus,

but apparently infiltrated the uterine wall to the extent of three-eighths of an inch. The mucosa surrounding the tumor was markedly hypertrophied. The tubes and ovaries did not show any pathologic alteration. The ovarian vein of the right side was distended by an organizing thrombus and a portion of this was protruding from the vessel after removal, as is shown in the accompanying drawing (Fig. 1).

Pathologic Histology.—On microscopic examination of stained sections of the growth several elements were found. The presence of chorionic villi in certain areas of the sections was decidedly marked, and a striking characteristic of these was the phenomenal, active disturbance of their cellular layers. In most of the villi the proliferation was most pronounced in the Langhan's cells (Figs. 2 and 3), and in many places these could be seen in several layers about the villi and apparently wandering in the acid-staining substance surrounding them. The cells varied in size, but all were moderately large and contained oval, well-defined, deeply-staining nuclei. In some of the cells active nuclear division was observed (Fig. 2).

The substance surrounding the villi stained deeply with the acid stains and resembled bands of fibrils and whorls of protoplasm. In many areas large, pale nuclei were found, and in the others pronounced vacuolization was observed. These protoplasmic masses were occasionally broken by spaces which were possibly blood channels, as many of them were filled with blood cells. In portions of the sections, collections of very large, oval and round cells were seen. These cells were invariably congregated in masses and, as a rule, were found on the borderline of the blood channels. They were, as I have stated, extremely large and contained rather large, oval and prominent nuclei. Their protoplasm, as a rule, was pale, and in many instances very ill defined. These cells had the general appearance of the decidual cells. In some areas of the tumor leucocytic infiltration was observed, though not to a great degree (Fig. 3).

Subsequent History.—The patient was living and well eight months after the operation, without any subjective manifestations of recurrence of the disease.

GENEALOGY OF CHORIOEPITHELIOMA.

This tumor had been diagnosed clinically as carcinoma of the corpus uteri, but on further investigation, particularly with the microscope, its true character was determined. The different terms applied to this comparatively rare condition of the uterine body are deciduoma malignum, malignant bladder mole, sarcoma deciduo cellulare, malignant placental polyp, and numerous other rather indefinite terms. These names were

applied to this growth in its early history, because it was thought in the earlier microscopic study of the growths that they were of decidual or maternal origin and belonged to the sarcoma family. The first important paper describing these tumors was contributed by Sanger¹ in 1889. At this time he described a case of malignant tumor of the corpus uteri possessing a sarcoma-like structure which followed an abortion at the eighth week. Sanger described this as a tumor belonging to the sarcoma family, developing from the decidua

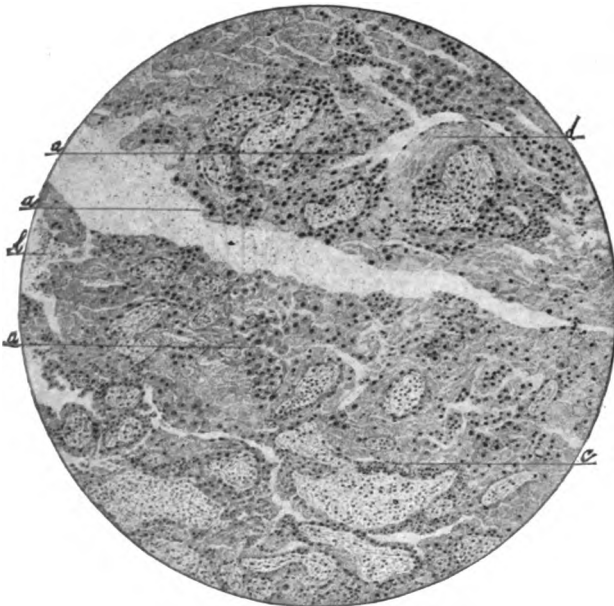


Fig. 2.—Low power microscopic section of tumor removed from its central portion. a, a, a, Large wandering decidual cells. b, Leucocytes. c, Chorionic villi showing marked disturbance in Langhans' cells. d, Non-nucleated protoplasmic masses.

and, therefore, he applied the term *deciduoma malignum*. Sanger² later collected all analogous cases from the literature, 11 in number, and these, with his own case, made 12. A paper describing these cases was published in 1893. Among the cases collected by Sanger

1. Sanger: *Centib. f. Gynak.*, No. 8, p. 132.

2. *Ib.*: *Arch. f. Gynak.*, vol. xlv, No. 1, 1893.

were 4 from the laboratory of Professor Chiari,³ who in 1887 described 3 of these growths, pronouncing them cases of uterine cancer complicating pregnancy. Gottschalk,⁴ in his contribution on the subject, possibly came nearer hitting the true character of these tumors as taught to-day. He described a case in which chorionic villi were present, and he found that there was quite marked cellular disturbance in the stroma of the villi and Langhan's cell layer. Therefore, he spoke of it as a sarcoma arising from the syncytium and Lang-

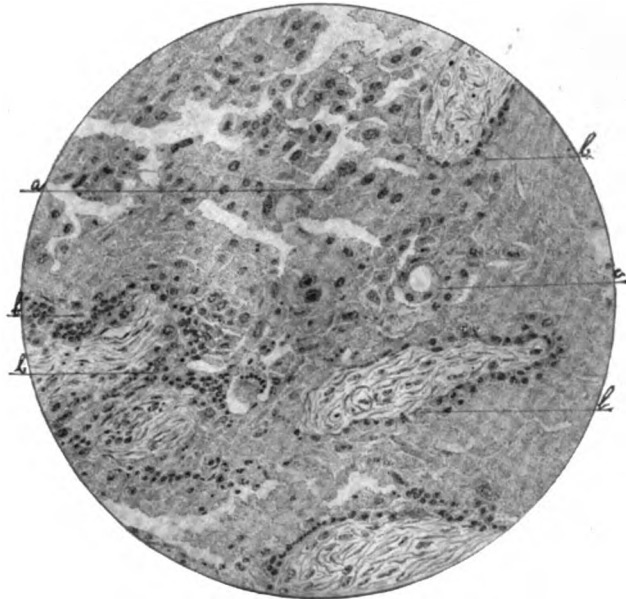


Fig. 3.—High power microscopic section removed from the tumor at its junction with the uterine structures. a, Collection of large decidual cells. b, b, b, b, Chorionic villi showing proliferation of their cellular covering. c, Large multinucleated cell containing a vacuole.

han's cell layer. Ludwig Frankel,⁵ however, was possibly the first man to describe the cellular origin of these tumors, and he undoubtedly was the first to ob-

3. Chiari: Wiener med. Jahr. der Kinderheilkunde Gesell. der Aerzte, vol. vii, 1887.

4. Gottschalk: Berliner klin. Woch., No. 4, 1893; Arch. f. Gynäk., vol. xvi, No. 1, 1894.

5. L. Fränkel: Arch. f. Gynäk., vol. xlviii, 1895.

serve the proliferation of the syncytium and of Langhan's cell layer. Sanger in his paper regarded the decidual cells as the important elements of the malignant tissue; the chorionic structure he thought foreign or totally adventitious. Sanger's paper, however, was the instrument which directed the attention of the profession to the study of these growths, and shortly after its publication, in 1893, the interest of the profession throughout the world was aroused and several similar cases were reported, particularly in Europe, and one by Williams⁶ in this country, in 1895.

Gottschalk, in 1894, published a paper in which he disapproved of Sanger's view of the maternal origin of these growths, and stated that he believed the disease arose primarily in the fetal tissues. From this assertion the old view of the destructive action of hydatidiform moles was revived; that is, that the fetal tissues have the power of invading and destroying the maternal structures. Frankel later (in 1895) reported a case of deciduoma malignum which he described as arising from the syncytium, a structure which he thought was derived from the uterine epithelium. In the same year, 1895, Marchand⁷ contributed an article claiming that these tumors originated in the two-celled covering of the chorionic villi. In the same year, Williams also recognized the relation of these growths to the chorionic epithelium. He recognized and described Langhan's layer of cells, but considered the syncytium the important element in the growth, and the latter, too, he was rather persuaded to believe of uterine origin. The writers of the present day nearly all seem to agree with the theory set forth by Marchand that these tumors are of chorionic, fetal or ovular origin. Many of the cases that were originally reported as malignant bladder mole, sarcoma of placenta, and sarcoma deciduo cellulare, etc., have been carefully re-examined and found to be true chorioepitheliomata. This work has been done since Marchand published his observations as to the character and origin of the "so-called decidual tumors and hydatid mole."

6. J. W. Williams: Johns Hopkins Hosp. Rep., vol. iv, No. 9, 1895.

7. Marchand: Monat. f. Geburt. u. Gynk., vol. i, June, 1895; Monograph, No. 1, 1903.

Veit,⁸ however, still continues to adhere to his original view that the disease is of maternal origin, and that a tumor of the character of the chorioepithelioma could not arise from fetal tissues. He therefore maintains that the old term deciduoma malignum is correct. He still claims, furthermore, that the primary disease is a sarcoma of the corpus uteri, which is cellularly modified, or given special features, such as syncytial conformation by some of the cells, by a superimposed pregnancy. In the strength of his argument, Veit cites the history of a tumor of this nature which he removed and which resembled strikingly a deciduoma. The tumor showed many villi with actively proliferating epithelium and many large cells (many polynucleated) in the circumjacent uterine tissues. These he regarded as sarcomatous cells of maternal origin and as the essential elements of the disease. The presence of villi Veit does not regard of importance, and he states that their existence is merely an accident of the existing gestation. Veit claims that he has never observed the infiltration of fetal elements. He would, however, regard the demonstrable infiltration and destruction of tissue by fetal cells as high evidence of malignancy. He also admits that the similarity between the large cells interspersed with the maternal tissues of the normal placenta, or an adjacent deciduoma, or the cells of the chorionic epithelium, or the cell masses of the tumor, are strikingly exact, but he does not believe, however, in the genetic continuity existing between the two.

As a rule, most late observers have but little difficulty in tracing the genesis of these cells. Teacher,⁹ in his discussion of chorioepithelioma before the London Obstetrical Society in 1903, stated that he was able in all his cases to demonstrate the origin of these cells very plainly. Furthermore, he asserted that he was able to demonstrate also their destructive action. The distinctive difference between Veit's and Marchand's theories, histologically, is that learned in the different significance attached to the cellular elements composing the tumor. Veit,¹⁰ in his paper on the deportation of

8. Veit: Volkmann's Sammlungen klin. Vort., No. 254, 1885; *Zeits. f. Geburt. u. Gynäk.*, vol. vi, 1886; *Zeits. f. Geburt. u. Gynäk.*, vol. xxxii, No. 1, 1895.

9. Teacher: *Trans. London Obs. Soc.*, June 8, 1903.

10. Veit: *Handbuch der Gynäk.*, vol. iii, No. 2, Wiesbaden, 1899, p. 533.

chorionic villi, eludes this question when he reaches the relation of that process to deciduoma malignum. Teacher, in personal conversation with Professor Veit, learned that, though he were forced to admit that these cells were not sarcoma cells of maternal origin but were derivatives of the chorionic epithelium, the theory which we now, in this country particularly, have almost generally accepted, he would, nevertheless, still hold that some pathologic condition inherent in the mother preceded the diseased condition of the ovum. This, Teacher, in his discussion before the London Obstetrical Society on chorioepithelioma, says may be even so, but, notwithstanding, it does not disprove that the elements which enter into the tumor formation are fetal.

Horrocks,¹¹ in discussing Dr. Teacher's paper, states that from his personal study of several cases of deciduoma malignum, he does not believe we are in a position at present to say that all cases are either of maternal or of fetal origin. He believes, with Lockyer¹² and others, that there are two kinds of malignant tumors associated with pregnancy: one of decidual (maternal) origin of the sarcomatous type, for which he thinks deciduoma malignum the proper term, and the other chorioepithelioma of fetal (ovular) origin of the carcinomatous type. This stand is taken by King¹³ in a paper read in Washington, February, 1904.

Marchand's theory is the one now most generally accepted, for he has demonstrated clearly the relation of the protoplasmic masses of the tumor with the syncytium and the relation of the individual cells with those of Langhan's layer. Peters¹⁴ also has observed the true genesis of the epithelial layers of the chorion. He demonstrated that the syncytium and Langhan's cells are derived from the ectoderm, therefore it follows that these tumors are undoubtedly entirely fetal or ovular in origin, and arise from a malignant proliferation of the two layers of the chorionic epithelium.

In reviewing the history of the so-called deciduoma malignum, I have found that the term had been applied to conditions of the uterus characterized by hyperplastic states of the decidua, to tumors of the decidual struc-

11. Peter Horrocks: Brit. Med. Jour., Oct. 5, 1902.

12. C. Lockyer: Trans. London Obst. Soc., January, 1902.

13. King: Trans. Washington, D. C., Obstet. Soc., February, 1903.

14. Peters: Centralb. f. Gynäk., No. 29, 1902.

ture, all of which were of unknown character, long before the publication of Sanger's paper, by Maier,¹⁵ Kustner,¹⁶ and Klotz.¹⁷ The malignant tumor, however, now under consideration, had never before the publication of Sanger's paper been definitely differentiated from other malignant tumors of the corpus uteri, and to him alone belongs the honor of pointing out their distinctive family relation. Gebhard reported 3 cases of chorioepithelioma in 1897; in all of these the characteristic cellular elements and syncytium were found present. The second case strikingly demonstrated the cellular origin of the tumor and in every way confirmed Marchand's theory regarding the genealogy and the relation of the tumor cells. Gebhard found in the wall of the uterus, far from the main growth in his second case, a villus from the surface of which the chorion or ectodermal cells could be demonstrated.

NOMENCLATURE.

With the genealogy of these growths definitely established, it would seem that their distinct relation and a definite terminology should be accepted universally; but even now, despite the almost universal acceptance of Marchand's theory as to the genesis of these tumors, there is still considerable discussion over the nomenclature of these growths, many investigators still clinging to the term *deciduoma malignum*, while others, and the majority, too, now accept the term *chorion epithelioma*, or, more recently, *chorioepithelioma*. Teacher considers syncytium a bad name, because the syncytium is not the characteristic element of the tumor. The most characteristic thing I have endeavored to point out in this paper is the physiologic prototype. Teacher, in his paper, favors the term which will indicate some origin of the tumor and believes that *chorioepithelioma malignum* is the best. He does, however, also favor allowing the term *deciduoma malignum* to remain as a clinical name. Moreover, the term, he says, has been so completely abandoned that it has ceased to be misleading.

PATHOLOGY. •

The tumor, as a rule, follows pregnancy, abortion, or

15. Maier: Arch. f. Gynak., vol. xxxiii, 1888.

16. Kustner: Arch. f. Gynak., vol. xxxiii, 1881.

17. Klotz: Arch. f. Gynak., vol. xlix, 1887.

the expulsion of an hydatidiform mole. Indeed, it has been learned that almost 50 per cent. of the cases of hydatidiform mole has been followed by chorioepithelioma. Metoz¹⁸ collected 98 cases of chorioepithelioma from the literature and found in this number 48 preceded by hydatidiform mole. In Teacher's collection of 188 cases, 73 were preceded by mole.

The tumor usually is situated within the uterine cavity, though cases have been reported where the growth has occurred primarily in the vagina. Again, it has occurred primarily in the Fallopian tube, following a tubal pregnancy. It has also been reported to have been observed primarily in the ovary, and also in the brain. These are all possibly cases in which deportation of the chorionic elements has occurred prior to labor, as almost every instance of cases thus recorded has occurred soon after parturition. Busse¹⁹ reported two cases of the disease in which the tumor developed primarily outside the uterus. In one it occurred in the left ventricle of the heart, with secondary deposits in the lungs, brain, kidneys, liver, spleen and intestines; in the other the disease developed in the parametrium, vagina and lungs, the uterus remaining entirely free. These may be instances of the deposition of elements of the chorion prior to the termination of the pregnancy, which developed a malignant change after its completion. Devitski²⁰ also reports a case of the condition occurring primarily in a virgin 75 years of age, with secondary growths in the lungs, liver and spleen. Steinert²¹ reports an instance of embryonal tumors of the genital glands occurring primarily in the testicle, containing pavement and cylindrical epithelium, smooth muscle fiber and chorioepitheliomatous elements, particularly the syncytium and Langan's cells. When the tumor is situated in the uterine body it is, as I have observed from my own case and from those recorded in the literature, situated in the fundal region and in the posterior wall. The growth varies in size; in some instances it can scarcely be palpated and in one case recorded it was felt as a simple scar, while in the same patient universal metastases were observed. Therefore,

18. Metoz: *Rev. de Gynecol.*, Paris, vols. iv and v, 1901.

19. Busse: *Virchow's Arch.*, Nov. 4, 1903.

20. Devitski: *Med. Obosreni*, vol. lvi, No. 5, 1904.

21. Steinert: *Virchow's Arch.*, Nov. 4, 1903.

the dimension of the growth does not in any way speak either of the benignity or malignancy of the tumor, but it would seem that those characterized by large size are less malignant and vicious than those of small size. The large tumors, too, usually contain chorionic villi, and these, as I have stated, appear to run a milder and calmer course than those of wholly cellular composition.

The tumor may be large, however, and may fill the entire uterine cavity, even dilating the interior to a considerable extent. Croom²² reports a case of chorio-epithelioma malignum in which the tumor weighed 7½ pounds. The uterus itself varies extremely in size. It may be small or apparently of normal size, depending, of course, on the size of the growth. In some of the cases which I have studied it extended to the umbilicus. The growth itself, in almost every instance, in the early stages is irregularly nodular. In this stage it is more or less firm and imparts to the tactile sense an impression of a fibroid tumor. Later, as hemorrhage takes place into the tumor substance, from the penetration of blood vessels by the chorionic villi, and the erosion of the vessel walls, it becomes softer and somewhat friable, and in the still later stages necrosis and sloughing take place, and then we simply find a scooped-out, sloughing ulcer occupying a site in the uterine wall.

In the early stages the growth confines itself to the superficial portion of the lining membrane of the uterus, though at no time is there a sharp line of demarcation between the malignant structure and the uterine wall, as is seen in placental polypus or in cases of retained placenta or membranes.

As the tumor ages, penetration of the mural portion of the uterus occurs, and even in the early stages on microscopic examination the wandering malignant cells will be found between the uterine muscular tissue, and penetration of the wall may take place. In a case recorded by Noble²³ and in one by Hirschman the uterine wall had been completely perforated and the wall of the bladder in each case was involved.

The tumor structure before necrosis and ulceration take place might conveniently be divided into three portions: The basal portion or that portion in juxtaposi-

22. Croom: *Med. Press and Cir.*, June 25, 1902.

23. Noble: *Amer. Jour. Obst.*, vol. xlvI, No. 3, 1902.

tion to the uterine structure, and the true, active, live portion of the growth; a second and middle portion or body which is composed of blood clot and necrotic tissue, wandering cells and fragments of chorionic villi; a third, the outer or free marginal portion or that portion free in the uterine cavity, composed of a capsule-like membrane. In the early stages this is of a smooth grayish-pink or grayish-green color, while the middle portion is more of a dark blood-coagula color.

METASTASIS.

One of the most remarkable characteristics of chorioepithelioma in the terminal stages and in some cases in the comparatively early stages, is the tendency to early metastasis to other viscera; and from the study of my collection of cases, in several instances, symptoms of metastases were the first manifestations of the disease, and suggested the possible existence of an intrauterine chorioepithelioma. In one patient the first evidence of the disease was cerebral irritation and later right-sided hemiplegia. In other cases the presence of the disease was first manifested by coughing, pleural pain and hemoptosis, thus indicating the presence of malignant emboli in the lungs. In several cases, too, the growth was first discovered in the labia and vaginal walls and the symptoms of the condition first directed to these structures. Of course the disease, as will be seen, occasionally apparently occurs primarily in these structures. The unusual tendency to widespread metastasis is undoubtedly due to the greatly increased vascularity in the organs of the pelvis, as a result of the pregnancy. The vessels, we know, at this time are multiplied and enlarged and, therefore, readily receive and convey the chorionic elements throughout the body. Of course, it is not improbable, as I have pointed out, that deposition of the chorionic structure takes place prior to the termination of the pregnancy.

LOCATION.

The tumor, as a rule, is primarily situated in the uterine cavity, though cases are recorded, 9 in number, in which the disease occurred primarily in the vagina. It may be primary, also, in the Fallopian tube, following a tubal pregnancy or tubal mole. The organs most frequently involved in metastatic deposits are the lungs, vagina, kidneys, liver, brain, spleen, ovaries, intestines,

broad ligaments, pleura, mesenteric glands, pancreas, heart, stomach, and pelvic lymphatic glands. Lymphatic gland infection, however, seems to be extremely rare. In my collection of cases, one instance is recorded in which the disease was first recognized by an apparent involvement of the left inguinal glands. This was first thought to be an adenitis, but incision into the tumefaction liberated a large quantity of bloody fluid, and sections taken from the diseased area showed the characteristic morphologic construction of the structure. In another case in my collection the pelvic lymphatic glands were involved. There are only 7 cases recorded in literature of lymphatic gland involvement; this, of course, is due to the fact that the malignant cells are invariably deported by the hemal circulation and rarely through the lymph channels. E. Seifert,²⁴ from his study of chorioepithelioma malignum, states that in those cases in which metastases are formed the brain is involved in about 10 per cent.

PATHOLOGIC HISTOLOGY.

On microscopic examination of these structures, different elements will be recognized. In some, nothing but large decidual cells, blood detritus and blood sluiceways will be found, while in others chorionic villi with their characteristic structure with proliferation of the Langhan's layer of cells and syncytium will be seen, a picture observed in my case. A characteristic of the cells is their great tendency to undergo modification. In certain areas, cells undergoing various degenerative changes will be noted, while in others a state of extreme cellular activity will be seen. Teacher says that in the study of chorioepithelioma it is very essential for proper appreciation to have material which shows the growing zone of the tumor and the stages of cell metaplasia or cell division. In such a part he states that three principal cell forms will be found: The syncytium, large masses of protoplasm of various shapes, rounded, drawn out bands and whorls or irregular masses. These are very frequently vacuolated and may contain blood, as will be noted in the case I have reported. These syncytia or so-called plasmodia contain numerous nuclei. In nearly all instances these will be found to stain deeply and uniformly. The protoplasm of the cells is opaque

24. E. Seifert: *Arch. f. Psych.*, No. 1, 1904.

and stains deeply with plasma stains. Karyokinetic figures are not found. Assemblages of cells are also seen growing in intimate relation with the syncytium. In the early stages the cells are small, well defined, and pack closely together. There is no stroma between them. The nuclei of these are round or oval and stain moderately deeply. Nuclear activity in these cells is always characteristically well marked. The protoplasm is pale and clear. In some cases it is delicate, too, and finely granular and stains but thinly with the plasmic stains. These cell masses are frequently found within the syncytium. They may show a border of syncytium resembling endothelium. A characteristic feature of the tumor on microscopic examination, in case the chorionic villi are present, is that the cells which I have described will be recognized as developing from the syncytium, the other cells from the second layer of cells covering the chorionic villi or Langhan's cells. Modifications and intermediate forms of the above cells, of course, are often seen.

The individual cell, Teacher claims, is rather the primitive form and the syncytium is a modification of it. He classifies the intermediate forms and the various infiltrating cells together as the first cell type. Teacher found the tumor cells usually assembled in masses of some size and attached to the uterine tissues. This is strikingly demonstrated in the case under my observation. These assemblages of cells are really the active portion of the tumor and the tissues external to these layers or collections of cells or that occupying the free uterine cavity is made up of lymphatic tissue and blood clot, as a rule; hence, the peculiar gross appearance of these tumors. The blood clot seems to be a characteristic feature of the growth, and it seems to be due to the growing and proliferating tumor eroding the vessels and causing hemorrhage into its substance proper. This is of the utmost importance, for in doing a test curettage for diagnostic purposes we often secure only the outer portion or degenerated portion of the growth, and, therefore, may be led astray as to the true character of the tumor on microscopic examination. It is important, therefore, in doing a curettage for diagnostic purposes to be sure of removing tissue in contact with the uterine wall. In the cell masses described under connective tissue, no blood vessels are present, as a rule.

LINE OF INVASION.

A peculiar and characteristic feature of chorioepithelioma is that the line of invasion differs distinctively from that of carcinoma. In chorioepithelioma the process is a destructive one, while in carcinoma there is usually a reactionary zone of inflammatory material and invading cells, giving rise to the indurated base, so characteristic of carcinomatous tumors. This, as you know, is nature's method of throwing up breastworks of defense to halt the invading army of malignant cells.

The relation of the degeneration of the muscular structure of the uterus to the tumor cells has been a subject for much discussion. In nearly all instances, some of the cells are found interspersed between muscular fibers in such a manner as to lead some investigators to believe that they are really degenerating muscle cells. It has been demonstrated, however, that true myomatous degeneration does occur and it is also firmly established, as I have pointed out in preceding paragraphs, that the neoplastic cells are found infiltrating between the muscle fibers, and it is by their action that fibrillar degeneration takes place. In my specimens I was able to locate a few choriomatous cells in the intermuscular spaces, but I did not recognize any degeneration of the muscle fibers.

OTHER NEOPLASMS CONTAINING CHORIOMATOUS CELLS.

In this connection, I desire to call attention to a class of tumors recently described as containing cells from the second layer of the chorionic villi, or Langan's cells, and in some instances also elements of the syncytium. These have been described under the terms embryomata, teratomata, etc. Pick²⁵ has recently described a tumor of this kind occurring in the ovary of a girl 9 years old, which he designates chorioepithelioma ectodermale. Landau reports 5 similar cases all occurring in young individuals. These growths were all vicious, and characterized, like the chorioepitheliomata, by early metastasis. Ritchie²⁶ described a tumor of this character occurring in the mediastinum of a man, and Andrews²⁷ reported a case of an endosteal

25. Pick: Berlin. klin. Wochst., No. 51, 1902.

26. Ritchie: Trans. London Obst. Soc., June 3, 1903.

27. Andrews: Trans. London Obst. Soc., June 16, 1903.

tumor of the femur, showing syncytial structures. Numerous other similar cases have been recorded. These tumors, as is known, are developed from the three embryonal layers.

Much discussion has arisen as to the proper classification of these growths. Fothergill²⁸ objects to the tendency of classifying these embryomata or tumors occurring in moles and others independently of pregnancy, but containing chorionic elements and the chorionic epithelium of pregnancy, under the same nomenclature. He says that even though they all be of fetal or of ovular origin it would be better to adopt a nomenclature which would distinguish those closely connected with gestation and those arising independently of it. He further says in support of his argument that "It is plain that a mother invaded by the trophoblast of her own child would be a person of one generation killed by the tumor in a person of the next generation—matricide, in fact—but a man killed by an embryoma of the testicle would be a victim, not of his own child, but a potential brother or sister, fratricide," a condition altogether different and worthy of an individual name.

ORIGIN OF THE SO-CALLED TERATOMATA.

Many theories are advanced as to the origin of these tumors, and we are still somewhat in the dark as to a proper classification, although these are the only growths of whose etiology we have a little certain knowledge. Galabin²⁹ does not believe that their derivation lies in an included ovum, a brother or sister of the unfortunate being who bears it. Such an imperfect or undeveloped being is usually, as is well known, attached to the surface, and there is no valid reason, he says, why they should be in the testis or ovaries. He believes that they are evidence of imperfect parthogenesis, or attempt at development of the germ elements without union of the sexes. This theory, however, is not considered by most authors, and the Marchand-Bonnet theory of fetal inclusion is now generally accepted. Pick and Landau also incline to this theory and they both have been able to trace the origin of these growths to the three embryonal layers. They found that, in some, certain layers would develop so rapidly as to completely

28. Fothergill: Trans. London Obst. Soc., June 16, 1903.

29. Galabin: Trans. London Obst. Soc., June 16, 1903.

obscure others, and for this reason the genesis of the teratomata was not properly understood. The existence of chorionic elements in certain cases of sarcoma has been set forth as an objection to deciduoma malignum. These, however, are found only in cases of embryomata, and this does not argue against their ovular origin, but favors the theory of deciduoma malignum, being derived from the elements of the fertilized ovum. It must be remembered, too, in this connection that Schmorl and Veit have shown that normal villi and fragments of chorionic epithelium are deported through the blood channels, either arteries or veins, to distant organs and there undergo destruction and become absorbed, or stop and give rise to a malignant neoplasm. This class of cases I have referred to. They were first brought to the attention of the profession in 1896 in the discussion of deciduoma malignum in the Obstetrical Society of London, in describing syncytial masses occurring in a malignant growth of the testis.

Schlagenhauser³⁰ later reported a case which was undoubtedly a teratoma, and this was one of the first theories advanced to destroy the theory of Marchand as to the origin of the chorioepithelioma. Schlagenhauser thought that a large proportion of the deciduomata occurring in the uterus and elsewhere should be regarded as teratomata, and due to the inclusion of an ovum.

ETIOLOGY.

In considering the etiology of chorioepithelioma or malignant disease arising from the chorionic epithelium, we are at once struck by the interesting phenomena associated with the causation of the condition. It is now thoroughly established that pregnancy is an absolutely essential factor in the production of these malignant tumors. It will be found in all cases thus far recorded that some form of gestation has preceded the malignant process, except in the case recorded by Pavlot³¹; and this tumor, we have learned, was of doubtful pathologic character. Ladinski³² says that there is no case recorded where the disease manifested itself outside the parturient age. In my collection of cases, however, I observed one instance of the malignant disease devel-

30. Schlagenhauser: Wiener klin. Wochft., Nos. 22 and 23, 1902.

31. Pavlot: Ann. de Gynecol., et d'Obst., vol. xli, 1904.

32. Ladinski: Amer. Jour. of Obst., April, 1902.

oping after the establishment of the menopause, the patient being 58 years of age.

In 128 cases collected by Ladinski, in which the nature of the pregnancy was recorded, 51 followed hydatid mole, 42 followed abortion, 28 followed labor at full term, 4 followed premature labor, and 3 followed tubal pregnancy. In 40 per cent. of these cases, therefore, it will be seen that the disease followed a molar pregnancy. In Williams' collection of 26 cases, 11 followed hydatid moles, 6 followed full-term pregnancy, 5 followed abortion, 1 followed tubal pregnancy, and in 3 of the pregnancies the true character of the pregnancies was not known. In the 198 cases collected from the literature by Teacher and reported before the Obstetrical Society of London in 1903, 73 followed mole, 59 followed abortion, 49 followed full-term pregnancy, and 7 followed tubal or ovarian pregnancy.

It is seen, therefore, that the relation of hydatidiform mole to chorioepithelioma is very significant, but the relation has not been satisfactorily explained. Hydatidiform mole itself is not, as first pointed out by Virchow, a myxomatous degeneration of the chorionic villi. It is, as more recently explained by Marchand, a proliferation of the syncytium and of Langan's cells, causing mechanical dropsy of the chorionic villi. The cause, however, of the formation of mole can not be definitely asserted to be due to pathologic changes either in the ovum or in the uterus. Chalensky is persuaded that the death of the embryo is brought about and the chorion, therefore, receives in consequence increased nutrition previously intended for the fetus, thus causing the proliferation of the chorionic elements. Marchand refutes this view on the ground that if this were the proper explanation molar pregnancy would occur more frequently. Ludwig Fränkel has brought forth the theory that ovarian adenocystomata must be considered as factors in the production of hydatid moles, as in a number of cases recorded bilateral ovarian adenocystomata were observed. This has been noted in 9 cases. Fränkel claims that in ovaries affected with cystic disease the activity of the corpus lutea and their secretion is destroyed, and that the influence of the latter being withdrawn from the ovum causes it to become diseased and to form a hydatid mole. Pick, however, asserts that in cystic disease of the ovaries there is an exces-

sive production of the lutein secretion, which is deleterious to the ovum and results in a hydatid formation.

Jaffe³³ also believes, with Pick, that the overproduction of corpus lutean secretion is one of the principal factors in the causation of this condition. He reports a case of ovarian tumor which developed 2 months after the discharge of a hydatid mole. This proved to be a chorioepithelioma. The right ovary, which was as large as an apple, showed the same structure. In both these tumors, multiple corpus lutea cysts were present, a condition which has been noted by many observers to accompany hydatid pregnancy. He believes, therefore, that there is a direct causal relation between the two conditions and states that an excess of corpus lutea material in the blood leads to the increase of trophoblasts, and hence the chorioepithelial development in the uterus. Recasens,³⁴ in considering the etiology, holds that the fetal ectodermal structures possess normal and specific malignant character, which, however, is generally neutralized by secretion of thyroid substance or secretion from the ovary. Therefore, if for any reason the normal secretion of these glands is arrested, abnormal development of the fetal structure occurs.

TIME OF OCCURRENCE.

It has been found that the average duration of time following the molar pregnancy and the manifestation of symptoms is about 4 months. This varies; in some of the cases in my collection the symptoms became manifest immediately after the expulsion of the growth; but the time of the development of the symptoms in all cases of molar pregnancy from my observation must be measured by days or weeks, not by months. In Ladinski's collection, the longest recorded time after the expulsion of the mole was nine months. Race has no influence in the development of the tumor; in cases from my collection it has occurred in all nationalities. Hydatid mole frequently follows an old endometritis. Menu³⁵ found only 12 cases in 79 in which a hydatid mole had occurred without a preceding childbirth in which the above condition existed.

33. Jaffe: *Arch. f. Gynäk.*, vol. lxx. No. 3. 1904.

34. Recasens: *Revista de Med. y Cir. Pract. Centralb. f. Gynäk.*, No. 18, 1904.

35. Menu: *Rev. de Gynecol.*, Paris, vols. iv and v. 1901.

Gottschalk, in discussing the pathogenesis of chorio-epithelioma, says that they are absolutely avascular, and states that the growth is nourished by osmosis from maternal venous channels into which the growth dips. He is persuaded, therefore, that this one-sided and exclusive nutrition with venous blood is the cause, the only important one, of the malignant transformations. He states furthermore that there is possibly an accumulation in the nuclein of the cell nuclei of substances having a chemically toxic action, which also acts as one of the fundamental causes in the production of this condition.

Herbert Snow,³⁶ in discussing the etiology, says that they may be growths due to altered cells of other malignant disease during preparation for study. He believes that the malignant process has already been grafted on the uterine wall before pregnancy takes place and that the malignant process does not follow that condition. Many others believe also in this same theory, for it was recognized in Williams' case that metastases were noticed in less than two weeks after a full term labor. This view, Teacher says, is not inconsistent with the development of the tumor after labor, for it is possible that thrombi could be carried into the parts containing malignant cells and tumor formation rapidly develop.

Another theory advanced as to the etiology of these malignant neoplasms is one fostered by Ehrlich's side-chain theory; that is, that an organism has the power to produce anti-cells or anti-bodies which are endowed with influences to prevent the excessive proliferation of chorionic elements and combat and render inert or destroy invading foreign cells, and, therefore, prevent chorionatous formation, but when the power of the patient to produce these bodies fails, undue proliferation of chorionic cells occurs and chorioepithelioma results. Veit and Scholten³⁷ have applied the term syncytiolysin to this body. Therefore, if during the pregnancy or labor chorionic cells or even portions of villi become detached and deported to other portions of the body, they disappear or are rendered entirely inert, provided the syncytiolysing power of the individual is normal. This theory would seem to explain the occurrence of

36. Herbert Snow: *Brit. Gyn. Jour.*, August, 1902.

37. Veit and Scholten: *Zelts. f. Geburt. u. Gynäk.*, vol. xlix, 1903.

cases of benign metastases, and also why metastases disappear after removal of the primary exciting focus. In this class of cases there is an excessive production and deportation of chorionic elements, which overwhelms the organism and destroys its syncytiolysing power, but after the removal of the provocative focus, and, therefore, after the withdrawal of the source of supply of the chorionic elements, the invaded organism recuperates, and anti-bodies are again rapidly manufactured, and attack and render innocuous the malignant deposits.

This theory would also seemingly explain those cases of spontaneous recovery reported. According to Ehrlich, the influence of these anti-bodies is not a specific one, and for the syncytial cells only, but for any bodies in which they find attractive receptors. The power of the anti-bodies seems to be to dissolve wandering embryonal cells and the dissolving influence of the syncytiolysins on the placenta has been demonstrated by Veit.

AGE.

It will be seen that in chorioepithelioma the disease becomes manifest earlier than any other form of malignant disease. Carcinoma and sarcoma, as is well known, occur near or after the menopause, though certain forms occur earlier, but the maximum incidence of carcinoma and sarcoma is near the menopause. The maximum incidence of chorioepithelioma, however, is in the second and third decades, as pointed out by Ladinski. His collection of 124 patients gave an average of 32 years. This corresponds, he says, to the generally accepted age of reproduction. The youngest patient observed in my collection of cases was 17 years; the case was one of tubal gestation and was reported by Marchand. The oldest patient in my number of cases collected was 58 years. The average age of women suffering from carcinoma of the uterus is stated as 54 years. It is seen, therefore, that age bears a direct influence in that the disease occurs during the active reproductive life. In nearly all my cases, the condition occurred in patients who had previously borne children, ranging from 1 to 11 labors. The average number of pregnancies recorded in a collection of 98 cases was 4.2.

The lapse of time between the termination of the pregnancy and the manifestation of the symptoms varies somewhat. In some cases the symptoms are pro-

gressive from the time of the labor. Indeed, in one case observed in my collection, symptoms began before the termination of the pregnancy, that is, bleeding. This, however, may simply have been a coincidence and not a manifestation of the disease. As I have stated before, however, the time in the majority of cases must be counted by days and weeks, not by months. One patient in my collection, who had one normal labor at the age of 26, was free from symptoms for 6 years before the disease manifested itself. In another patient of 24, the disease did not begin until two and one-half years after the completion of a normal pregnancy. The duration of the time existing between the completion of the labor, whether it be mole, abortion or normal labor, and the evidence of symptoms does not seem to be influenced either by a mole pregnancy, an abortion or a normal pregnancy. The average lapse of time in Ladinski's collection of cases was 8 weeks, 7 weeks and 5 weeks after a mole pregnancy, abortion, or a labor at term, respectively. McCann²⁸ also reports a case occurring after the menopause. Marchand explains these phenomena of a long period of latency by citing the fact that portions of epidermis are often included in the closure of some of the embryonic clefts. These, as we know, may remain quiescent, 10 or even 20 years, and then, for some unaccountable reason, suddenly spring into activity and form neoplasms. Marchand thinks, therefore, that it is not strange to find the trophoblast lying dormant for a varying period of years and then suddenly becoming active. Croom found in cases he collected from the literature that the average time for the development of symptoms after normal labor was 6.9 weeks; after abortion, 11.4 weeks; after mole, 10 weeks.

MALIGNANCY.

An interesting question in the study of chorioepithelioma, and one which is not perfectly understood, is why these growths vary so greatly in malignancy. In some cases we find the patient succumbing before operative interference is instituted, or the mother of a few days or a few weeks, while in others we find that the patient recovers after a simple curettement, and, indeed, in some spontaneous healing is asserted to have oc-

28. McCann: Brit. Obst. and Gyn. Jour., No. 281, 1901.

curred, and in others, despite the evidence of metastatic deposits in other viscera, we find patients recovering after radical operation. In the large majority of cases, however, we find that the behavior of chorioepithelioma is characterized by the highest type of malignancy. Death is usually the ultimate result. It is found that in cases in which villi are present a lower degree of malignancy exists. It is further stated that primary growths in the vagina are less malignant than when located in the uterus, though from the study of my cases this assertion does not hold good. In 9 cases reported in which the tumor was located primarily in the vagina, early dissolution occurred in all. Another question of extreme interest is why metastases should disappear after the removal of the primary exciting focus and why, as in cases reported by Noble and Herschmann, partial removal of the primary growth should be followed by the disappearance of portions which have infiltrated, as in Noble's case, the bladder wall, and which could not be removed. These phenomena are possibly explained by Ehrlich's side-chain theory. McCann, in his study of cases, believes the polypoid or circumscribed form of the chorioepithelioma less malignant. I believe this inference to be drawn from the fact that a tumor presenting such a conformation is only observed in its incipency, and, therefore, if proper treatment be instituted, a good result may obtain.

CLINICAL SYMPTOMS.

In describing the symptoms of chorioepithelioma we might conveniently divide them into two stages: 1, the incipient and formative stage; 2, the terminal stage or stage of metastasis and absorption. The symptoms in the incipient stage of the disease are first manifested by bleeding. This is an invariable symptom and usually is the first to attract attention. It appears without any cause, and is very irregular. In some instances it may be scanty, while in others it may be extremely profuse and serious. A characteristic of the bleeding of chorioepithelioma is that it is not alleviated by ordinary means of treatment. In all the cases in my collection the patients were, in almost every instance, curetted, and this seemed only to aggravate the condition, or only to control it temporarily. In one or two cases a simple attempt at examination was followed by extensive hemorrhage and profound collapse, the

hemorrhage being controlled and the life of the patient saved only by immediate packing and resort to stimulation. The hemorrhage in some instances is continuous, while in others it appears at irregular intervals and varies in quantity. During the period of quiescence, a thin, watery discharge is usually complained of. As the disease progresses, bleeding becomes more pronounced from the erosion of the vessels. Necrosis of the tumor takes place and a foul, profuse discharge is present. In the early cases reported, pain was not recorded as a symptom, but in the later observations this was almost invariably present. It is of a crampy, boring character, situated in the lower portion of the abdomen. In my own case, and also in the case recorded by Ladinski, in April, 1902, pain was the first symptom complained of. Anemia and emaciation are quite marked in all. In the case under my observation the patient had lost several pounds before admission to the hospital. Prostration is also quite profound.

In the second stage, the stage of metastasis and absorption, all these symptoms become more pronounced. Should involvement of the lung, which is the most frequent organ affected by metastatic deposits, occur, pain, cough, hemoptosis and pleural friction sound and areas of consolidation may be manifest. Metastatic deposits in the brain would be evidenced in the first stage by cerebral irritation, later by paralysis. Deposits in the kidney give rise to pain, and possibly to hematuria. During the absorption stage there are, of course, taken into the human economy products of necrosis, and therefore symptoms of sepsis and exhaustion, such as sweating, elevation of temperature from 100 F. to 103 F., rapid pulse, nausea and vomiting will be present.

In the terminal stages of the disease, malignant cachexia also becomes quite marked. If penetration of the uterine wall occurs, the bladder or rectum may become involved, and, therefore, symptoms referable to these organs will be present.

PHYSICAL SIGNS AND DIAGNOSIS.

The diagnosis of chorioepithelioma from our present knowledge of the condition should be comparatively easy. Taking into consideration the characteristics of the preceding clinical history of a normal labor, abortion or tubal pregnancy, or molar labor, followed by the symptoms above enumerated, should lead to the

suspicion of the disease. This, combined with the bimanual examination and a test excision of a portion of the tumor, would undoubtedly establish the true character of the lesion. We should not, however, depend on the microscope alone, for simply finding syncytial masses in curetted material after a mole labor, abortion or normal labor, does not necessarily indicate the presence of chorioepithelioma. Particular attention should be paid to the clinical symptoms and physical signs. In the early stages of the condition, the uterus is found to be somewhat enlarged. This may vary, according to the age of the tumor, from merely normal size to the tumor reaching almost to the umbilicus. The uterine wall is somewhat softer than normal and softer in consistence than if due to the presence of a fibroid tumor. Of course, in the early stages, the consistence of the uterus would not be affected; it is only when the disease extends into and destroys the mural portion of the organ that its consistence would be altered. In nearly all the cases recorded the os uteri is found dilated, admitting, as a rule, one finger, and in some instances two fingers. The growth in some instances is found to be smooth, and nodular, while in others it may be more or less uniform and present as a simple nodule in the uterine wall, or as a soft scooped-out ulcer. As I have already stated, the tumor, as a rule, is situated in the fundal portion and posterior wall. This, from the cases I have collected, seems almost characteristic of the growth. The consistence of the growth varies; in the early stages it may be more or less moderately firm, but later, as hemorrhage and necrosis take place, it becomes friable, and in the terminal stages, when necrosis is complete, the tumor itself may have totally disappeared and nothing but a scooped-out, sloughing ulcer will be found in the uterine wall. It seems to project from or, in fact, infiltrate the wall, or, in other words, it is a portion of the uterine structure, and bleeds on the slightest provocation. It could readily be differentiated from a submucous fibroid by the history of the case, by the characteristic feel, and, finally, by microscopic examination. It would be differentiated from a carcinoma by the clinical history and by the consistence of the mass, particularly the basal portion of the mass. In carcinoma it would be hard and indurated, while in chorioepithelioma it is a soft, sloughing ulcer.

Lastly, microscopic examination of sections of the tissue would reveal their true character. In sarcoma of the corpus uteri it would be differentiated by the clinical history, by the rapidity of growth and by microscopic examination. The metastatic deposits observed resemble to a large degree hematomata, but these on microscopic examination, as a rule, will be found to contain the characteristic elements of the growth.

PROGNOSIS.

The prognosis of chorioepithelioma is extremely grave. It is perhaps the most malignant of all tumors, occurring as it does during the full physiologic activity of the patient and with the physiologic process of pregnancy, in an organ in which at this time the blood vessels are greatly multiplied and enlarged, and, therefore, in a condition highly favorable to the transportation of these malignant cells to other portions of the body. The prognosis would seem to be somewhat modified by the character of the growth, for, as I have pointed out, in certain forms of chorioepitheliomata the tendency toward malignancy is not as marked as in others, those we find containing chorionic villi being less malignant than those without these elements. In 124 cases recorded by Ladinski there were 51 recoveries and 73 deaths, giving a mortality of 59 per cent. In 66 patients operated on radically, 57 by vaginal hysterectomy, 6 by abdominal hysterectomy, 3 by laparotomy, 50 of these recovered. Dorland's⁹⁹ 52 cases recorded in 1897 gave a mortality of 73 per cent. In Teacher's 188 cases, 99 patients were treated by radical operation. In 87 there was either no operation or it was not radical. Out of the last number 83 died. The fate of 2 was not known. In 2, spontaneous healing occurred. Of 36 deaths, 11 occurred within a few days, and 25 after longer intervals. Of the patients operated on, 16 showed no improvement, 9 made a good recovery. In 5 several months of good health were enjoyed before recurrence. In 5 patients only did the disease recur after more than 6-month intervals. Of the 63 recoveries, 32 patients were well 6 months after the operation, 24 of these after 1 year, 13 after 2 years. Of the patients who had shown signs of disease in the lungs, 8 operated on recovered; in 2 others

39. Dorland: *Univ. Med. Mag.*, No. 8, vol. ix, 1897.

there were growths in the vagina and 1 in the ovary. In 3 of the cases operated on incomplete operation was done, but the patients recovered. Death usually results from metastases, hemorrhage, exhaustion and sepsis. In 210 cases of hydatidiform mole collected by Findley⁴⁰ there were 49 deaths, a mortality of 25 per cent. Of this number, 32 patients died from chorioepithelioma.

Metastasis, however, must not be considered a contraindication to operation unless the patient's condition is in extremis, for several cases are recorded in which recovery occurred where metastatic deposits had been quite marked. The disappearance of metastasis after radical operation is explained by the fact that the malignant cells can only live in live blood and not in extravasated blood; wherever metastatic deposits occur, hernial extravasation occurs and they are, as it were, responsible for their own destruction.

TREATMENT.

The treatment of chorioepithelioma should be the same as for malignant disease elsewhere in the body—complete extirpation of the uterus in the field of healthy tissue at the earliest possible moment should be the only operative resource considered. If we knew more, however, of the early development of chorioepithelioma, preventive means possibly could be instituted. In cases of hydatid mole, however, precautionary measures can be successfully adopted. Bonnaire insists that every woman who has had a hydatidiform mole should be regarded as menaced with malignant disease. After a molar labor, the uterus should be thoroughly cleaned and packed to induce the uterine muscle to contract and thus to regain its consistence and thickness. Bonnaire⁴¹ recommends that the cavity of the uterus be swabbed with creosote or with zinc chlorid and that the uterus should, at the interval of 10 or 15 days, be curetted and the curetted material subjected to microscopic study. Findley recommends the same procedure. If, after these operations, atypical metrorrhagia persists, inoculation of the uterus with malignant elements should be considered probable, and the organ should be removed, even if unable to detect any intrauterine

40. Findley: *Amer. Jour. Med. Sci.*, No. 8, vol. cxxv, 1903.

41. Bonnaire: *Rev. de Gynecol.*, Paris, vols. iv and v, 1901.

nodule or ulceration, by digital palpation or by microscopic examination of the scrapings. In every case of this condition the uterine cavity should be thoroughly cleaned of all elements of this tissue. This should be subjected to careful microscopic examination and should any atypical proliferation of the cells of the villi or suspicious curetted material be seen, early hysterectomy should be performed. I am indebted to Dr. E. E. Montgomery for the privilege of reporting this case.

A STUDY OF THE MESENTERIC GLANDS IN THEIR RELATIONS TO TUBERCULOSIS.

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THIS investigation involved a study of the mesenteric glands in 70 cases, divided into two principal groups, the tuberculous and the non-tuberculous. The tuberculous group numbered 49, and included those in which a distinct tuberculous focus or foci, great or small in extent, could be demonstrated somewhere in the body. The non-tuberculous group numbered 21, and included those in which it was impossible by gross examination to demonstrate in any part of the body a tuberculous lesion.

The mesenteric glands were placed under three headings: (1) the apparently normal, (2) the enlarged, and (3) the tuberculous. The normal glands need no comment. Under the enlarged glands (a rather indefinite term) were included all those in which no changes other than an increase in size and perhaps softening could be demonstrated. As the glands in infants and children are normally relatively large, they were not denominated as such, unless the increase in size was marked. The tuberculous glands included all those which were grossly the seat of tuberculosis, whether tubercle bacilli could be found in spreads or not.

Of the 49 tuberculous cases, 6 were of pulmonary tuberculosis with normal mesenteric glands; 1 was a case of pulmonary and intestinal tuberculosis with normal mesenteric glands; 7 were of pulmonary tuberculosis with enlarged mesenteric glands; 9 were of pulmonary and intestinal tuberculosis with enlarged mesenteric glands; 5 were of pulmonary tuberculosis with tuberculous mesenteric glands; 14 were of pulmonary and intestinal tuberculosis with tuberculous mesenteric glands; 5 were of general miliary tuberculosis with enlarged mesenteric glands; 1 was a case of tuberculosis of the bronchial lymph nodes with enlarged mesenteric glands, and 1 was a case of primary intestinal tuberculosis with terminal general miliary tuberculosis and tuberculous mesenteric glands.

The mesenteric glands, then, were normal in 7, enlarged in 22, and tuberculous in 20 of the 49 cases in the tuberculous group. In nearly 60 per cent. the glands showed no gross evidence of tuberculosis. Of the 25 cases in which there were both pulmonary and intestinal lesions, 60 per cent. of the glands were tuberculous. Of the 18 cases in which there were pulmonary but no intestinal lesions, about 28 per cent. of the glands were tuberculous.

In all cases cover-glass spreads were made from the glands, and examined for tubercle bacilli. Of the 49 cases of the tuberculous group, tubercle bacilli were found in 25 and could not be demonstrated in 24. The bacilli found possessed the morphological and tinctorial properties of the human tubercle bacillus.

Of the 25 cases of the tuberculous group showing bacilli in spreads from the mesenteric glands, 1 was a case of pulmonary and intestinal tuberculosis with normal mesenteric glands; 2 were of pulmonary tuberculosis with enlarged mesenteric glands, without intestinal lesions; 5 were of pulmonary and intestinal tuberculosis with enlarged mesenteric glands; 5 were of pulmonary tuberculosis with tuberculous mesenteric glands, without intestinal lesions; 11 were of pulmonary and intestinal tuberculosis with tuberculous mesenteric glands; while 1 was a case of primary intestinal tuberculosis with terminal miliary tuberculosis and tuberculous mesenteric glands.

Thus, 36 per cent. of the glands showing tubercle bacilli in spreads gave no gross evidence of tuberculosis.

Of the 24 cases of the tuberculous group not showing tubercle bacilli in spreads from the mesenteric glands, 6 were of pulmonary tuberculosis with normal mesenteric glands; 4 were of pulmonary tuberculosis with enlarged mesenteric glands; 5 were of pulmonary and intestinal tuberculosis with enlarged mesenteric glands; 3 were of pulmonary and intestinal tuberculosis with tuberculous mesenteric glands; 5 were of general miliary tuberculosis with enlarged mesenteric glands, and 1 was a case of tuberculosis of the bronchial lymph nodes with enlarged mesenteric glands.

In this latter group of cases, in which tubercle bacilli could not be demonstrated in spreads from the mesenteric glands, a further test of the tuberculous infectivity of the glands was made by stripping the capsules, macerating the pulp in bouillon and injecting 1 to 2 c.c. of this suspension into the peritoneal cavity of guinea-pigs. Nine of these animals died in from twenty-four to forty-eight hours after the injection, and nothing could be ascertained regarding the tuberculous properties of the corresponding glands used. Of the remaining 15 pigs, 2 died in three and four weeks respectively, and 14 were killed in six weeks. Of these 13, 12 showed marked tuberculous lesions in the liver, spleen, lungs, and occasionally the peritoneum. In a number of these lesions tubercle bacilli were demonstrated. The one guinea-pig failing to show tuberculosis was injected

from a case in which the only tuberculous lesion was an old healed scar at the apex of one lung.

Thus, $87\frac{1}{2}$ per cent. of the 24 cases of the tuberculous group not showing tubercle bacilli in spreads gave no gross evidence of tuberculosis, while the infectivity of these glands on animals was shown in 15 out of 16, or $93\frac{1}{2}$ per cent. of cases. Or, taking the whole tuberculous group of 49 cases and ignoring the 9 cases in which the inoculated pigs died early, 39 out of 40 cases, or over 97 per cent., gave evidence of tuberculosis, though in 60 per cent. of cases the glands gave no gross evidence of the disease.

The relations between the finding of tubercle bacilli in spreads from the glands and evident tuberculous lesions in the 49 cases, are conveniently noted by observing that there were 6 cases of pulmonary tuberculosis with normal mesenteric glands, none of which showed tubercle bacilli; 1 case of pulmonary and intestinal tuberculosis with normal mesenteric glands, in which no tubercle bacilli were found; 7 of pulmonary tuberculosis with enlarged mesenteric glands, 3 showing and 4 not showing tubercle bacilli; 9 of pulmonary and intestinal tuberculosis with enlarged mesenteric glands, 4 showing and 5 not showing tubercle bacilli; 5 instances of pulmonary tuberculosis with tuberculous mesenteric glands, all of which showed tubercle bacilli; 14 of pulmonary and intestinal tuberculosis with tuberculous mesenteric glands, 11 showing and 3 not showing tubercle bacilli; 5 cases of general miliary tuberculosis with enlarged mesenteric glands, none of which exhibited tubercle bacilli; 1 of tuberculosis of the bronchial lymph nodes with enlarged mesenteric glands, tubercle bacilli not being demonstrable; and 1 instance of primary intestinal tuberculosis, with terminal general miliary tuberculosis and tuberculous mesenteric glands, in which tubercle bacilli were found.

The non-tuberculous group, in which it was impossible to demonstrate by gross examination tuberculous lesions in any part of the body, included 21 cases. These died from a variety of causes, among which were diseases especially liable to cause enlargement of the mesenteric glands, such as typhoid fever and bacillary dysentery. The glands were apparently normal in 6 and enlarged in 15 instances. Of the 21 cases 10 were children. In 9 of these 10 the glands were enlarged. In the 11 adult cases there were 6 instances of gland enlargement. As far as the results here obtained point, however, the size of the glands is probably of little importance; and the enlargement in so many cases in children was due to the fact that most of them died of ileocolitis.

The mesenteric glands in the non-tuberculous group were all examined for tubercle bacilli, but the spreads gave negative results.

The glands from each case were then macerated in bouillon and inoculated into guinea-pigs, as in certain of the tuberculous cases. Of the pigs injected 6 died within forty-eight hours, and these

cases were not considered. The 15 animals that survived were killed six weeks after the dates of inoculation: 6 of the pigs showed distinct tuberculous lesions in the liver, spleen, and lungs; 8 gave negative results; and 1 was doubtful, exhibiting only a few pinhead-sized foci in the liver. This last case was ignored.

Thus, in a little over 40 per cent. of cases the mesenteric glands of the non-tuberculous group were shown to contain matter capable of producing tuberculous lesions in guinea-pigs. Of the 14 cases in which the test was satisfactorily carried out, 9 were adults and 5 were children. Of the adults, 4 gave positive and 5 negative results. Of the children, 2 gave positive and 3 negative results. The division is thus fairly even. That enlargement of the glands alone bore little relation to the results obtained is shown by the facts that in the children's cases the glands were enlarged in all 5 instances, 2 giving positive and 3 negative results, and that in the adults' cases the glands were normal in 4 and enlarged in 5 instances, 2 of the former (4) giving positive and 2 negative results, while 2 of the latter (5) gave positive and 3 negative results. The ages of the children are of some interest, as is also the fact that all of them were hospital cases and bottle-fed. The 2 children giving positive results were two and nine months old respectively, and died of ileocolitis. The 3 children giving negative results were one, two, and nine months old respectively. It is also worthy of note that 2 cases of typhoid fever in adults gave negative results.

Was the tuberculous infectivity of the lymph glands of the mesentery, as shown in 97 per cent. of the tuberculous and 40 per cent. of the non-tuberculous cases, peculiar to them? Or was it shared by the other lymph nodes of the body? Were the parenchymatous organs also involved? An attempt was made to answer these questions by a few experiments along lines similar to those followed in the study of the mesenteric glands.

The enlarged axillary glands from a case of chronic pulmonary tuberculosis were tested for tuberculosis by examination of spreads and inoculation of a guinea-pig. The spreads showed no tubercle bacilli, but the pig developed marked tuberculous lesions of the spleen, liver, lung, and peritoneum.

The apparently normal inguinal glands from a case of general miliary tuberculosis in a ten months' infant were tested in the same way. The spreads showed no tubercle bacilli, but the pig developed tuberculosis in the spleen and liver.

The slightly enlarged inguinal glands, obtained from an adult without the slightest gross evidence of tuberculosis anywhere in the body, were inoculated into a guinea-pig. The animal was killed in six weeks and showed marked tuberculous lesions of the liver, spleen, and lungs.

Portions of the spleen, liver, and kidney obtained from a case of chronic pulmonary tuberculosis, but showing no gross evidence of

tuberculosis themselves, were inoculated into guinea-pigs. All the animals developed very marked tuberculous lesions in the spleen, liver, and lungs.

Portions of spleen, liver, and kidney were likewise obtained from a case showing no tuberculous lesions in any part of the body, and used for similar inoculations. The pigs injected were killed at the end of six weeks, and were found to be free from tuberculosis.

These few cases do not warrant positive conclusions, but they suggest rather strongly that the tuberculous infectivity of the mesenteric glands is common to gland groups in other parts of the body. The importance of this point lies in the logical supposition that involvement of the mesenteric group alone would mean infection from the intestines, while general involvement of the lymph nodes throughout the body would indicate hematogenic infection. The results obtained from inoculations with portions of the spleen, liver, and kidney also offer the suggestion that, while the lymph glands throughout the body are commonly the harbor of tuberculous material in the tuberculous, and perhaps the non-tuberculous, the parenchymatous organs are only involved when tuberculous lesions are present somewhere in the body. The evidence on this point, however, is too meagre for the suggestion to be of any value without further studies.

The extent of the lesions found in the infected pigs possesses some points of interest. A few pigs were inoculated with distinctly tuberculous glands of the mesentery in which tubercle bacilli had been demonstrated in spreads, and these died in from three to four weeks with very extensive lesions. The pigs inoculated with glands from tuberculous subjects, in which, however, no tubercle bacilli had been demonstrated, were killed at the end of six weeks (with two exceptions), and showed lesions less marked than the preceding animals. The pigs developing tuberculous lesions after inoculation from non-tuberculous cases showed, on the whole, the least extensive lesions. The pigs inoculated from the inguinal and axillary glands exhibited quite marked lesions. The animals inoculated with spleen, liver, and kidney of the tuberculosis case showed the most extensive lesions of all. Except in the cases where the pigs were infected with glands showing tubercle bacilli, and the spleen, liver, and kidney of the tuberculosis case, the animals gained weight progressively, contrary to what would be expected.

Controls were furnished all through the investigation by the pigs dying within forty-eight hours of the peritoneal injection. These numbered fifteen. In none of them were tuberculous lesions found.

CONCLUSIONS. 1. In all cases of active tuberculosis, and in almost all cases of inactive tuberculosis, the mesenteric glands are tuberculously infective.

2. The mesenteric glands in these cases may or may not show gross evidence of tuberculosis or tubercle bacilli in spreads; the

result is the same as far as the qualitative production of tuberculosis is concerned.

3. The mesenteric glands, in a certain percentage of cases showing no tuberculous lesions in any part of the body, are tuberculously infective. In the present study the percentage was about 40.

4. The tuberculous infectivity of the mesenteric glands is probably shared by the other groups of lymph nodes throughout the body.

The material used in the experiments was obtained by the writer from the Henry Phipps Institute, during his service as pathologist to the institution, from the Philadelphia Hospital, and from private cases.

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THE ACTION OF ACID-FAST BACILLI WHEN INOCULATED INTO THE PERITONEAL CAVITY OF WHITE RATS.

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Numerous observers, experimenting with acid-fast bacilli, have produced marked tuberculiform nodules in various animals, especially when the inoculated bacteria were reinforced or augmented by sterile oil or butter. Intravenous inoculations have given rise to nodules in the kidney, with ray forms of the organism resembling actinomycetes, while subcutaneous methods have developed abscesses. Calves and rabbits are very suitable animals for inoculation experiments, the guineapig proving more or less refractory to these organisms.

Courmont and Potet,¹ through subcutaneous inoculation of various acid-fast bacteria, conclude that it may be followed by abscess formation with recovery of a bacillus, which tends to lose its acid-fast property. By the subcutaneous injection of doses of 7 cc. of a liquid culture, Courmont and Descos obtained, after 30 days, in addition to local abscesses, tuberculiform nodules of the lungs; the latter consisted of inflammatory tissue, but contained no giant cells. The results of intraperitoneal inoculations depend upon whether they are given pure or with sterile butter. When the latter method is used, according to Rabinowitsch, death occurs in from two to four weeks. Autopsy showed peritonitis, adenitis of mesenteric glands, sometimes attended by necrosis, and false membrane agglutinating the organs, while granulation nodules, more or less numerous, were scattered throughout. Acid-fast bacilli were isolated from the lesions, but giant cells were not observed.

Mayer² asserts that the lesions are first exudative, then inflammatory. When butter is inoculated with the bacilli, the irritation produced by the former generates epithelioid cells surrounded by fibrin. Holscher

is said to have seen neither extension, caseation nor actinomycotic forms with the Petri-Rabinowitch bacillus or the organisms from grain. On the contrary, Mayer with the timothy bacillus obtained true caseation and giant cells in tubercles. Intraperitoneal inoculations of pure cultures were sometimes followed by septicemia. Inoculations of chickens and pigeons with Korn's bacillus No. 2 are followed by negative results, while white mice react positively with No. 1 and negatively with No. 2. Tobler's bacillus No. 1 in white mice produced fatal septicemia with tuberculiform nodules in the peritoneum without caseation and giant cells. The timothy bacillus inoculated intraperitoneally in rabbits produces death in four or five weeks, sometimes from septicemia, together with the formation of whitish nodules on the omentum, liver, and peritoneal adhesions and development of cavities in the lungs. Microscopic examination of the nodules shows epithelioid cells, some resembling giant cells. In rabbits the lesions are the same, with the exception that the nuclei of the giant cells are not placed so near the periphery as in those found in human tuberculosis.

Schultz and Lubarsch inoculated acid-fast bacteria into the kidneys of rabbits and 13 days later found ray forms resembling actinomyces. Subcutaneous inoculation was followed by a local abscess only, while intraperitoneal inoculation gave rise to peritonitis and tuberculiform nodules. Visceral involvement may take place if the dose is large.

Abbott and Gildersleeve¹ found that after subcutaneous inoculation into rabbits or guineapigs, of from .5 cc. to 1 cc. of opaque suspension, there is, as a rule, either no result or suppuration (subacute) of the neighboring lymph-nodes. If pure cultures be injected into the peritoneal cavity and the dose be not excessive, *i. e.*, not more than 1 cc. of an opaque suspension, there is often no result; but if there is injected a small quantity of some such irritant as sterile butter, and this is followed by an injection of the bacteria in pure culture, an extensive, sometimes fatal, fibrinopurulent peritonitis results. By injecting directly into the testicles of guineapigs with the view of forcing the bacilli into the abdominal cavity, the results may be negative or suppuration may occur at the site of injection.

If, on the other hand, sterile butter be injected into the peritoneum of an animal so treated, there is usually a widespread fibrinopurulent peritonitis, in addition to

nodular formations containing acid-fast bacteria. Intravenous injections are preferred by these observers for studying the pathogenic possibilities of this group of bacteria. The lungs rarely showed involvement, as in 45 rabbits inoculated intravenously, pulmonary lesions were observed in only seven; 23 of these were inoculated with Moeller's grass bacillus No. 2, and the lungs of two were involved.

Of 11 inoculated with the Petri-Rabinowitsch bacillus, "suspicious nodules were found in the lungs of one" while in 11 others treated with Moeller's timothy bacillus, involvement of the lungs was present in four. In each of four rabbits inoculated with genuine tubercle bacilli there was marked pulmonary involvement. Not in a single one of the foregoing experiments with acid-resisting bacteria was involvement of the liver, spleen, myocardium, or diaphragm observed.

Hogs which received 2 cc. of a thick suspension of Moeller's grass bacillus No. 2, were killed 55, 70, and 75 days after inoculation, and only in one were lesions found which contained acid-resisting bacteria. The third animal received in addition to the subcutaneous injection, a second dose of 13 cc. of a suspension of the same organism directly into the lung. The latter organ was free from nodules, and only a few adhesions were present at the site of the inoculations. The bacterium was obtained in pure culture from the adhesions in this case, as well as in a fourth animal treated in the same manner. Cultures from the internal organs of all four animals were negative, except in the lungs of animals three and four.

Six calves were inoculated intravenously with acid-resisting bacteria, three with the timothy hay bacillus of Moeller, and three with the butter bacillus of Petri-Rabinowitsch. The amount of inoculation was the entire surface growth of two well-developed agar slant cultures which had grown for six days at 37° C., and four days at ordinary room temperature. None of the animals gave evidence during life of inconvenience from the inoculation. Two animals were killed on the twenty-second, and four on the thirty-third day after inoculation. In not a single instance did the autopsy reveal the presence of lesions that could be referred to the bacteria inoculated, and the blood and internal organs, as determined by cultures, were free from living bacteria. Nine calves inoculated into the pulmonary structure with the same bacteria, failed to produce a condition simulating tuberculosis.

In the nodules of those animals inoculated intravenously they assert that it is possible to detect in serial sections, hyphæ or club-like forms of the organisms, and claim that "it is evident that this is the normal mode of development of these organisms in the tissues." The actinomyces developing from the butter bacillus (Rabinowitsch) and from the grass bacillus, No. 2 (Moeller), are often much smaller, more delicate, and less numerous than are those from the timothy hay bacillus (Moeller), which is more prone to involution forms.

The histologic picture corresponds more to the suppurative and exudative change than to the proliferative and progressive necrotic reactions peculiar to true tuberculous infections, and this difference becomes more and more evident as time advances. No tendency to progressive destruction of tissue through the fusion of neighboring nodules, so characteristic of tuberculosis, takes place.

Abbott and Gildersleeve claim, in conclusion, and it is the opinion of others, that there can be little doubt of a botanic relationship between the so-called bacillus of tuberculosis and the so-called acid-resisting bacilli, the ray fungi known to us in connection with actinomyces of man and animals, and some of the so-called streptothrices concerned in the condition known as pseudotuberculosis.

Sato and Brauer inoculated two calves intraperitoneally with 100 cc. of a bouillon culture of an acid-proof bacillus, obtained by them from butter. One calf received, in addition to the culture, 100 cc. of melted sterile butter. In the calf which received the butter, plus the culture, three large tumors resembling granulomas were found in the peritoneal cavity, while in the animal which received only the bouillon culture, no lesions were present.

Moeller⁴ records a few experiments upon calves with the bacillus of human and bovine tuberculosis and pseudotubercle bacilli. A calf of 5 weeks was fed for three months upon boiled milk, to which was added 12 cc. of sputum containing tubercle bacilli. At the end of this time it was inoculated, intraperitoneally, with 6 cc. of a 1 to 50 bouillon dilution of the human tubercle bacillus. At the site of inoculation, there developed a tumor, which later broke down; the softened material contained numerous tubercle bacilli, which proved fatal to two guineapigs. The abscess healed, the animal gained weight, and after 208 days it was killed. At the

site of inoculation, was found a tumor the size of a "walnut," in which tubercle bacilli were demonstrated. All the other organs were normal. A guineapig inoculated with macerated tissue of the tumor, contracted general tuberculosis, and died in three weeks.

A second calf, aged 16 weeks, was inoculated intraperitoneally once a week for three weeks with 12 cc. of a culture of the tubercle bacillus in sterile butter. At the site of inoculation there appeared a tumor the size of a "goose egg" which was hard and firm. The animal gained weight and after 102 days was killed. Upon autopsy the peritoneal layers (parietal and visceral) contained small grayish-yellow nodules about the size of a "grain of wheat." In the mesentery and the parietal layer of the omentum were many nodules the size of a "lentil" and some as large as a "hazel nut;" a few were yellowish in color and firm, others were yellowish-red, soft and gelatinous. In the omentum, areas of coalesced nodules resembling cauliflower formation were present, while upon the liver and spleen, broad sessile masses were observed. Adhesions of the visceral layer of the omentum together with adhesions between the liver, spleen, and diaphragm were quite marked. The bronchial, mediastinal, intercostal, mesenteric and sternal glands were enlarged and swollen. Two guineapigs inoculated with the macerated gland structure contracted tuberculosis and died. A third calf aged 7 weeks, was inoculated intraperitoneally once a week for three weeks with an eight-day old culture of the pseudotubercle bacillus. The animal gained weight and after 102 days was killed. There was no tumor formation at the site of inoculation and all the organs and tissues were normal. A fourth calf aged 6 weeks, was inoculated intraperitoneally once a week for three weeks with 10 cc. of a culture of the pseudotubercle bacillus (bovine) mixed with sterile butter. A tumor, the size of a "fist," appeared at the site of inoculation, but at the end of five weeks had disappeared. The animal gained weight, and after 113 days was killed. The same lesions were present as in calf number two, and the bacillus was demonstrable in sections and spreads.

A fifth calf, aged 2½ months, was inoculated once a week for three weeks with 10 cc. of an 8-day old bouillon culture of the grass bacillus. No lesions were found at autopsy, which was held 101 days after the first inoculation.

Calf No. 6, aged 3 weeks, was treated the same as

the preceding animals, except that in addition to the bacterium, sterile butter was inoculated. After 128 days the animal was killed. Nodules of various sizes, some firm, others soft, were found in the peritoneum. The liver and spleen showed upon their superior surface an opaque nontranslucent deposit which was adherent to the diaphragm. The mesenteric glands were enlarged and the grass bacillus was obtained in pure culture.

Moeller, in conclusion, states that the injection of the human tubercle bacillus or the grass bacillus without butter has no effect upon calves, while if injected with butter, both produce the same effect.

The following personal experiments were undertaken to determine if lesions could be produced in the white rat by various acid-fast bacteria without the addition of sterile oil or butter. All the inoculations were made into the peritoneal cavity and a 5-weeks old agar culture rubbed up in bouillon was used in all bases. The animals were killed with chloroform, some in 30 days and others after the lapse of 54 days. It can be readily seen by referring to the detailed experiments that nodules or tubercles were constantly produced in the peritoneal cavity and in one or two cases nodules were produced in the parenchyma of the liver. Though the pancreas in these animals is extremely small, segments of this organ adjacent to sections of liver or spleen showed lesions histologically similar to the nodules found in the peritoneum. It will be further noticed that the heart, lungs, kidneys and intestines remained exempt from the infection. In one instance nodules were implanted upon the kidney, but did not extend into the parenchyma of the organ. In one case a nodule was present in the serous coat of the stomach and extended into the muscular coat.

Histologically the nodules in all the animals were identical, being made up of large, more or less oval, slightly granular cells; lymphocytes, spindle-shaped cells, and polynuclear leukocytes. In some sections were cells possessing 10 to 12 nuclei, for the most part peripheral, the others being in the center of the cell. Newly formed tissue was evidenced by the presence of a large number of small bloodvessels and blood sinuses limited by the cells already mentioned, principally the oval and spindle-shaped cells. In some of the masses small foci made up entirely of polynuclear elements and suggesting pyogenic infection were present. Areas of coagulation necrosis were also prominent. Caseous foci

noticed at autopsy were found to be made up of polynuclear leukocytes and a granular detritus, which did not react to acid dyes, but took the basic stain quite decidedly. Free nuclei of polynuclear leukocytes were also scattered throughout. Even the pancreas showed cellular infiltration and areas of coagulation necrosis. In the splenic nodules the large oval cells were very abundant, most of them possessing a single nucleus, crescentic in shape, while others contained two or three such nuclei.

None of the animals showed illness or emaciation at any time and they apparently would have lived indefinitely. Similar experiments upon guineapigs were entirely negative. The bacilli were easily demonstrable in the sections and still retained their resistance to 25% sulfuric acid, but in morphology they were distinctly changed. Instead of being from 2 microns to 4 microns in length, they averaged about $1\frac{1}{2}$ microns, were quite plump and were scattered widely throughout the tissue. No club-shaped form or any tendency to form rays, as noticed by Abbott and Gildersleeve in kidneys of rabbits inoculated intravenously with acid-fast bacteria, were demonstrable. In some specimens, as many as eight to ten bacilli were found in the large oval cells, but most of the organisms were extracellular. In cultures the bacilli regained their natural morphologic characters and exhibited their usual resistance to acids. Cultures obtained from the lesions produced the same phenomena in a second series of white rats. The sections were stained with hematoxylin and Van Gieson, and hematoxylin and eosin for histologic studies, while for acid-fast bacilli they were stained with carbol fuchsin and counterstained with Gabbet's solution.

Following are the details of the experiments:

RAT No. 1.—Inoculated with Korn's grass bacillus No. 2. Weight at time of inoculation, 280 gm.; at death, 290 gm. The peritoneal cavity contained 30 cc. of slightly cloudy fluid. Small nodules were present around the spleen, in the mesentery, and between the stomach and liver. The nodules varied between 3 mm. and 8 mm. in diameter, and were quite firm with the exception of one near the stomach, which was apparently caseous(?). One small nodule was found upon the sixth rib, and upon section contained a few calcareous areas. Spreads and cultures from both the fluid and the nodules contained acid-fast bacteria in pure culture.

RAT No. 2.—Inoculated with Rabinowitsch's butter bacillus. Weight at time of inoculation, 305 gm.; at death, 305 gm. In the abdominal wall corresponding to the site of inoculation were three closely grouped, firm, pinkish-white nodules, 2 mm. in diameter. There were no nodules in any other portion of

the body. Spreads made from the cut surface of the nodules contained acid-fast bacilli, but cultures were negative.

RAT No. 3.—Inoculated with the horse-dung bacillus. Weight at time of inoculation, 235 gm.; at time of death, 240 gm. In the peritoneal cavity were a few recent adhesions, as well as a few scattered nodules. Some of the nodules had coalesced, while others were isolated. The individual masses were from 2 mm. to 5 mm. in diameter. Upon the superior surface of the diaphragm were small nodules ranging in size from 3 mm. to 5 mm. None were caseous. Several masses were seen upon the stomach and several upon the liver. Spreads and cultures were positive for acid-fast bacilli.

RAT No. 4.—Inoculated with the butter bacillus of Grassberger. Weight at time of inoculation 90 gm.; at death 185 gm. Scattered throughout the peritoneal cavity were numerous small nodules of a whitish color. A few small masses were present upon the inferior surfaces of the liver and diaphragm. Recent adhesions were present between the diaphragm and the liver. None of the masses was more than 5 mm. in diameter. In addition to the lesions just mentioned, a small cyst, which contained a tapeworm 30 cm. in length, was present in the liver. Spreads and inoculations from the lesions contained acid-fast bacteria.

RAT No. 5.—Inoculated with Moeller's grass bacillus No. 2. Weight at time of inoculation 210 gm.; at death 212 gm. Upon the abdominal wall at the site of inoculation numerous small nodules were present. Throughout the peritoneum were many spheric masses varying from 5 mm. to .5 cm. in diameter, most of them firm and dense, while some were quite soft and resembled caseous material. A few firm nodules were also observed around the liver and spleen and upon the inferior surface of the diaphragm. Spreads and cultures were positive for acid-fast bacilli.

RAT No. 6.—Inoculated with the mist bacillus. Weight at time of inoculation 212 gm.; at death 220 gm. Upon the belly wall small, firm nodules were found. Small, firm masses were abundant in the peritoneum; some were present in the liver, others between the liver and the stomach and between the spleen and stomach, ranging in size from 5 mm. to 1 cm. in diameter. Intimately adherent to the small intestines was a firm, grayish-white mass, irregularly nodular, measuring 1.5 cm. in length and 8 mm. in thickness. The left testicle was enlarged, swollen and adherent: upon section it was caseous (?). Spreads and inoculations from all the lesions contained acid-fast bacteria.

RAT No. 7.—Inoculated with the margarin bacillus. Weight at time of inoculation, 209 gm.; at death, 198 gm. Numerous very firm nodules were observed in the peritoneum, especially in the region of the liver and spleen, and few were seen in the hepatic structure. A few adhesions extended from the nodules upon the liver to similar structures upon the inferior surface of the diaphragm. These nodules varied from 3 mm. to 5 mm. in diameter. No bacteria were obtained either from spreads or in cultures.

RAT No. 8.—Inoculated with the blindschleichen bacillus. Weight at time of inoculation, 130 gm.; at time of death, 182 gm. Two nodules, one caseous, were found in the abdominal wall near the site of inoculation. There were numerous tubercles in the peritoneum from 3 mm. to 6 mm. in diameter, none of which was caseous. Around the spleen and between the liver

and stomach nodules were also evident. Acid-fast bacilli were obtained both in spreads and cultures.

RAT No. 9.—Inoculated with *B. tuberculosis piscum*. Weight at time of inoculation, 215 gm.; at death, 225 gm. Scattered throughout the peritoneal cavity were nodules varying in size from 5 mm. to 1 cm., some firm and fibrous, others caseous. The right kidney was adherent to the right lobe of the liver, and showed numerous whitish nodules upon its surface. Tubercles were also present between the liver and stomach, and between the latter organ and the spleen. Imbedded in the liver parenchyma were several small nodules 3 mm. to 5 mm. in diameter. The under surface of the diaphragm was completely studded with small firm tubercles, 2 mm. to 4 mm. in diameter. Acid-fast bacilli were obtained in spreads and cultures.

RAT No. 10.—Inoculated with the grass bacillus of Korn, No. 2. Weight at time of inoculation, 210 gm.; at death, 220 gm. Only a few small masses were present in the peritoneal cavity, and one large nodule, 1.5 cm. in diameter, the center of which was distinctly caseous. A few nodules, ranging in size from 2 mm. to 6 mm., were also present between the liver and stomach and around the spleen. Spreads and cultures contained acid-fast bacilli.

RAT No. 11.—Inoculated with the grass bacillus of Moeller, No. 1. Weight at time of inoculation, 185 gm.; at time of death, 200 gm. Nodules were abundant in the peritoneal cavity, and a small number were also seen in the liver and around the spleen. The under surface of the diaphragm contained a few masses, none caseous. No acid-fast bacilli were obtained in cultures or in spreads.

RAT No. 12.—Inoculated with Karlinski's bacillus. Weight at time of inoculation, 195 gm.; at death, 210 gm. In the peritoneal cavity was a large agglutinated mass made of small, firm, grayish-white nodules, extending about the liver, stomach and spleen. Tubercles were observed upon the inferior surface of the diaphragm and in the liver, but none showed signs of softening. Acid-fast bacilli were obtained in cultures and spreads.

RAT No. 13.—Inoculated with the milch bacillus. Weight at time of inoculation, 200 gm.; at death, 210 gm. The abdominal wall contained a small nodule near the site of inoculation. The peritoneum contained a few small nodules; none was caseous and none measured more than 4 mm. in diameter. A small number of masses were present around the spleen and between the liver and stomach. Cultures and spreads were entirely negative for acid-fast bacilli.

From these notes, it will be observed, that tubercles or tuberculiform nodules were produced in every case, and in one instance there was effusion into the peritoneal cavity. To me, the naked-eye appearances of these lesions resemble those of similar lesions brought about by tubercle bacilli, and only by cultures and histologic examination can the true nature of the processes be determined. True caseation was not constant, and when this degeneration did take place, the substance formed did not respond to stains, as does the caseous material in a frank tuberculous process, due to true tubercle bacilli.

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CONTRIBUTION TO THE STUDY OF SYPHILITIC SPIROCHÆTAS IN CEREBROSPINAL FLUID.

BY

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(From the Jefferson College Laboratories.)

The discovery of spirochætas in primary specific lesions by Schaudinn and Hoffmann¹ undoubtedly announces a new era in our studies of syphilis. The presence of the spirillums was verified and corroborated by a certain number of competent observers, as Metchnikoff and Roux, of Pasteur Institute, and others. The future experiments will determine, if the spirochætas are the only pathogenic agents of those various specific manifestations which accompany or follow even many years later an initial chancre. The discovery of various serums which are antitoxic in character has brought remarkable results in combating certain infectious conditions. Syphilis is due to an infection, and if the infectious element is discovered there is a bright outlook for its culture, and development of an antitoxin. As it stands at present, no attempts as yet have been made in that direction; observers are only studying the presence of the spirillum in specific lesions.

The effect of syphilis on the nervous system is very great. The damage it produces in the delicate structures of brain and cord is well known. Cerebrospinal syphilis is certainly a very common affection. Although we have powerful means for combating some of its manifestations, we nevertheless often fail in our efforts. If mercury and iodids could be brought into immediate and intimate contact with the nervous elements, perhaps therapeutic results would be more brilliant. In the light

of the new discovery, it is probable that if mercury and iodids which are antagonistic to syphilitic lesions, have an antagonistic effect on the syphilitic spirochætas great results could be obtained by direct application of mercury or iodids to the spirochætas. The cerebrospinal tissue is directly inaccessible, but the cerebrospinal fluid can be easily reached. Are the spirochætas present in this fluid?

With this object in view I made a series of investigations. Selection was made of patients with cerebrospinal syphilis and tabes, who presented an undoubted history of syphilis. Lumbar punctures were performed with all possible antiseptic precautions at the level of the fourth and fifth lumbar vertebrae. In each case 4 cc. of clear fluid was obtained and the tubes placed in a centrifuge. The centrifugation lasted from a half hour to two hours. Drops taken from the bottom of each tube were examined very carefully with an oil immersion lens, also several spreads were made from each case and stained according to Marino's method,¹ as strongly advised by Metchnikoff and Roux.² Of all the 10 cases examined, 8 presented cerebrospinal symptoms many years after the initial lesion. The most careful and repeated examinations of the unstained and stained specimens failed to reveal the presence of spirochætas in the 8 cases. It then appeared to me interesting to see whether they are present in the cerebrospinal fluid of patients with initial lesions. Two patients were offered to me by Prof. Horwitz, to whom I am indebted for this privilege. One presented a syphilitic chancre of 12 days' duration and the other of four weeks'. While in the first case the spirochætas were absent, in the second, bodies were found which resembled somewhat some of the varieties presented on the drawings of Schaudinn's article. The brief histories of the eight cases are as follows:

CASE I.—W. H. E., aged 62, presented upon examination cerebral and spinal symptoms: Headache, mental hebetude, impairment of memory, ataxia, spasticity, exaggerated knee-jerk, Babinski and paradoxical reflexes on both sides; disturbance of micturition and defecation. Previous history of chancre with secondary eruption 15 years ago. Diagnosis: Cerebrospinal syphilis.

CASE II.—C. R., aged 29. Chancre at the age of 19. Five weeks ago, subsequently to an insignificant trauma, developed: Ataxia, spasticity, exaggerated knee-jerks with Babinski and paradoxical reflexes on one side, difficulty of micturition and sexual impotence, sensory disturbances marked. Diagnosis: Specific myelitis.

CASE III.—Wm. M., man, aged 49. Chancre with secondary symptoms 20 years ago. Presents a history of a left hemiplegia

three years ago, from which he recovered under mercurial treatment. A year later a similar attack and recovery. One year ago attack of aphasia, from which he recovered, when put on mercurial treatment. Two months ago a right hemiplegia with left homonymous hemianopsia. Patient also has paroxysms of severe headache and mercury is the only drug that relieves him. Diagnosis: Cerebral syphilis.

CASE IV.—C. McN., aged 34. Chancre with secondary symptoms seven years ago. Present, ataxia, exaggerated knee-jerks, Babinski reflex on one side, paradoxical reflex on the other; involvement of rectum and bladder. Diagnosis: Syphilis of the cord.

CASE V.—Mrs. L., aged 40. History of six miscarriages and two stillborn children. Says husband had an eruption several years ago, which lasted about four weeks; lost his hair at that time. Patient presents a thickening of sternomastoid muscle, a peripheral facial palsy, intense headache, which can be relieved only with mercurial inunctions; also exaggerated knee-jerks, bladder disturbances. Diagnosis: Cerebrospinal syphilis.

CASE VI.—C. T., aged 38. Chancre with secondary symptoms 14 years ago. Came to the Jefferson Hospital with a left facial palsy, a palsy of two branches of the fifth nerve (complete anaesthesia over the entire distribution of these two nerves); also a neuroparalytic keratitis of the left eye with involvement of the third nerve on the opposite side. There was also a history of nocturnal headache unusually severe in character. The knee-jerks were much exaggerated; ataxia of the lower extremities; finally, involvement of the sphincters complete the picture. Diagnosis: Cerebrospinal syphilis with multiple palsies of the cranial nerves.

CASE VII.—C. C., aged 34. Chancre 10 years ago. He presents ataxia of lower and upper extremities, exaggerated reflexes and Babinski, involvement of sphincters and some cerebral symptoms, namely, headache, impairment of memory, and attacks of confusion.

Diagnosis: Cerebrospinal syphilis.

CASE VIII.—H. D., aged 29. Chancre nine years ago, with secondary symptoms seven years later. Ataxia with sharp shooting pains in the lower limbs. A year later difficulty of micturition. At the same time dimness of vision. Now he presents: Ataxic gait, Romberg's sign, loss of reflexes, Argyll-Robertson pupils, optic neuritis.

Diagnosis: Tabes.

CONCLUSIONS.

The absence of spirochætas in the cerebrospinal fluid in the eight cases with cerebrospinal symptoms suggests the thought that perhaps in parasyphilitic lesions which are tertiary manifestations of lues there is only a *chronic intoxication* produced by a toxic product elaborated by the spirochætas. Metchnikoff and Roux assert that positive results are obtainable only in the primary lesions. McWeeney⁴ has also obtained positive results in primary lesions, but failed to find the spirochætas in advanced tertiary ulcerations.

I wish to acknowledge my gratitude to Professor W.

M. L. Coplin for many valuable suggestions. I am indebted to Dr. Bland for the lumbar punctures in the first three cases.

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⁴British Medical Journal, June 10, 1905.

*THE USE OF THE ANTITOXIN OF DIPH-
THERIA IN THE TREATMENT OF
CEREBROSPINAL MENINGITIS.*

BY RANDLE C. ROSENBERGER, M.D., PHILADELPHIA.

The employment of the antitoxin of diphtheria in the treatment of cerebrospinal meningitis is attracting a great deal of attention, not only from the clinician but from the bacteriologist. As to its curative effects too few cases have been treated to give a definite opinion. According to specificity, it seems improbable that a definite or specific reaction occurs. It might, however, represent a bactericidal action of the blood serum.

When a rabbit, guinea-pig, horse, or any animal, including man, receives inoculations of a specific substance, the body becomes so accustomed to it that in time the substance produces no effect either locally or systemically.

The specific substance may be a bacterial poison (a toxin), blood from another species, a chemical, a vegetable poison, or it may be bacteria in a dead or living condition. Repeated inoculations will finally bring the body to a state of immunity. This condition is due to the formation in the fluids of the body, and especially the blood serum, of a substance (or substances) causing certain reactions when brought in contact with the materials or cells used to bring about immunity.

Take, for example, a rabbit inoculated repeatedly with human blood. The serum of this animal when brought in contact with human blood, or fluids containing human blood, will cause a precipitation and

disintegration of the blood cells—cytolysis. Take the serum of this same rabbit and bring it in contact with the blood of a healthy rabbit, and no such reaction takes place.

Inoculate a guinea-pig with the blood of a rabbit, and in the serum of the pig there is developed a substance (or substances) which destroys the red cells of the rabbit's blood, but will not destroy or alter in any way the blood of another guinea-pig. Let us use ricin to inoculate an animal, at first in very small, non-poisonous doses, and gradually increase the dose and frequency of inoculation until an extremely toxic dose is administered. The animal becomes immune to the poison, and in its blood there is formed a substance which is distinctly antagonistic to ricin—antiricin.

Now let us use the toxin of the bacillus of diphtheria and inoculate an animal, first with non-lethal doses, and increase the amount gradually until we bring about such a condition of immunity that enormous doses can be withstood, even when injected into the circulation. In the blood serum of such an animal is developed a substance which acts directly against the toxin, an antitoxin. It does not exert this effect upon all toxins—*i.e.*, those elaborated by other bacteria. In other words, the substance which is formed in the body of an animal immunized is specific only for the substance with which it was inoculated.

All of these substances, whether produced by the inoculation of blood, of bacteria, of toxin, or vegetable poison, belong to a group of substances termed antibodies. The action of each is, so to speak, specific, and each is formed by a definite

chemical union. If there is no union brought about, we will not have any antibodies formed. As to the antitoxin of the bacillus of diphtheria, this substance acts specifically against the toxin of the bacillus of diphtheria. It does not kill the bacillus, but, as the name indicates, it neutralizes the toxin, thus inhibiting systemic poisoning. If we had the streptococcus pyogenes or the pneumococcus as the causative factor in the production of a pseudomembranous process which resembles the one produced by the bacillus of diphtheria, we would not expect the antitoxin of diphtheria to cure this affection. Instead of using the antitoxin of diphtheria we would resort to what is known as an antimicrobial serum, one which acts against a specific bacterium, and hence would administer antistreptococcus or antipneumococcus serum. The reason is that we wish to destroy the bacteria, and not neutralize the toxin. Further, we know that the streptococcus and the pneumococcus frequently find their way into the general blood-supply, causing bacteremia, and this fact also prompts us to use an agent that will destroy the bacteria. We would not use an antistaphylococcus serum for a streptococcic or pneumococcic process, but we must use a specific substance in each particular case. In diphtheria, the bacillus remains distinctly localized where the pseudomembrane has formed, and only on the rarest occasions is this organism found in the blood during life. We do not resort to an antimicrobial serum, but knowing that the bacillus is constantly elaborating a toxin, we administer an antitoxin.

As to cerebrospinal meningitis, this

malady is generally conceded to be due to the meningococcus of Weichselbaum. At the present time there is no antitoxin for the toxin of this organism. If the disease is due to a specific bacterium, then a specific serum, an antitoxic or antimicrobial one, should be used in the treatment of the malady.

According to the latest theory of immunity (Ehrlich's) there must be some suitable receptor or side-chain existing in the body before antibodies are formed. This is well illustrated by taking the toxin of the bacillus of diphtheria. When this substance is elaborated and diffused through the system (if the latter is at par) there is a combination of the toxin with the suitable receptor, and this union brings about the formation of the immune body. If there is no suitable receptor present, then no chemical reaction takes place, because the receptor must have some assimilable foodstuff—i.e., toxin.

There is therefore no good reason to believe that antidiphtheritic serum can be of value in cerebrospinal meningitis.

A CABINET FOR INVESTIGATING THE ACTION OF VAPORIZABLE AND GASEOUS DISINFECTANTS AND INSECTICIDES, AND FOR TEACHING DIS- INFECTION TO STUDENTS.¹

BY

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This cabinet is a rectangular compartment 1 meter (40 in.)² in width, 1 meter (40 in.) in height, and 1.5 meters (60 in.) in length, constructed of wood and glass. The wood frame is of dressed yellow pine, 4 cm. (1½ in.) square, solidly framed together and resting on a table 67 cm. (27 in.) in height. The glass is bedded in putty and secured in position by strips of wood; the bottom of the case at its junction with the table, as well as the doors, is rendered as tight as possible by the use of rubber-edged weather strips. Upon one side are two doors, each 30 cm. (13 in.) wide and 90 cm. (36 in.) in height, hinged and closed so as to afford as accurate coaptation as possible. One of these doors fastens on the inside with two bolts, the other closes and locks to the first, and is supplied with an ordinary door knob of a kind usually applied to the doors of dwelling houses, and like them, removable for the introduction of the discharge tube from a formalin generator. At one end there is another door, which it was thought might be useful for the introduction and removal of anything after the connections with the formalin generator had been made by the device already indicated; it could have been omitted without imperiling the value of the device. The top of the case is also panelled and glazed, thereby fully lighting its interior; if for any reason it is desired to darken the case, a light-proof rubber cloth is thrown over and around it.

At one end of the case is a flat shelf 15 cm. (6 in.) in width, for the reception of petri dishes, test solutions, etc. Just below this is a second shelf, inclined at such an angle that tubes containing bouillon may be laid upon it without spilling the fluid or moistening the cotton plugs which may be left in place. The

¹Read before the Pathological Society of Philadelphia, October 27, 1904.

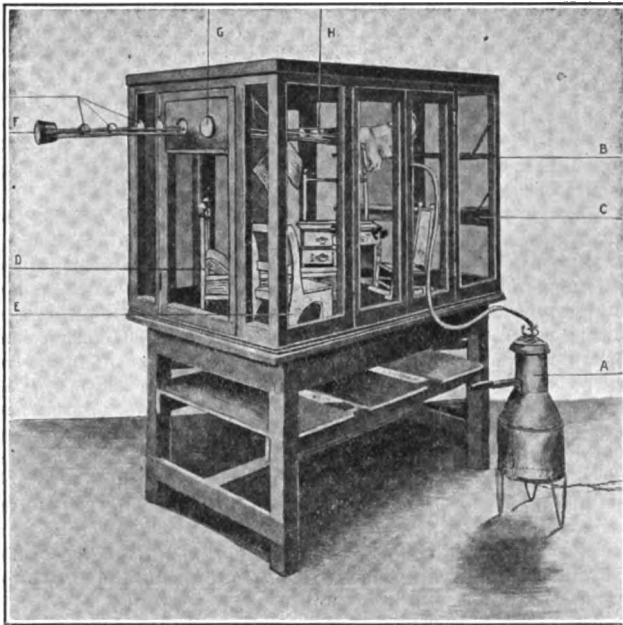
²The metric equivalents in inches given in this article are approximate.

interior of the cabinet is supplied with a complete set of doll's furniture, consisting of bed, mattress, pillows, the necessary linen, an ordinary chair, a rocking chair, and a bureau; the drawers and side compartment of the latter contain the trousseau necessary for a young lady of her social position.

In one end of the case, shown in the accompanying illustration, occupying the upper portion of the door, is a device for the introduction of test objects and also for their removal during disinfection of the chamber. This device is made in duplicate, both parts being exactly alike. It consists of a board 5 cm. (2 in.) in thickness, set in the upper part of the door, and perforated by two openings each 7 cm. (3 in.) in diameter, through which passes a movable carrier, each end of which is supplied by a conical wooden plug that can be made to engage in the circular opening so as to secure a practically air-tight closure. This carrier is 60 cm. (24 in.) in length, and consists of five round, wooden rods, so set into the small ends of the plugs that together they form a tray, in which can be deposited pill boxes, small petri dishes and bottles or tubes, the diameters of which do not exceed that of the opening through which the carrier passes. When out and loaded, the carrier can be forced into position in the fraction of a second, or can be withdrawn from the interior in the same length of time. As both ends of the carrier terminate in conical plugs that tightly fit the opening, the latter is always closed, except during the brief interval necessary for pushing the carrier in or pulling it out. When pulled out, the opening is closed by the inner plug, and when pushed in, by the outer plug. Were I reconstructing this device, I should so arrange it that one carrier would be at the upper and the other at the lower end of the door. The cabinet should be longer, certainly 2 meters (80 in.) and so constructed that it could be placed on end or flat to meet special indications. I do not recall any publication describing a similar device, but Dr. M. J. Rosenau, Director of the Hygienic Laboratory of the United States Public Health and Marine-Hospital Service, has applied essentially the same principle to the wall of a small room in which experiments on disinfection are conducted; although we had used the disinfection chamber for several years, the device for securing removable test objects was based on a rather imperfect recollection of Dr. Rosenau's apparatus.

For instructing the class in the principles of disinfection the following steps are necessary. The two side doors are opened, giving free access to the interior; it is then explained that in actual practice, before entering the room the individual having charge of the disinfection would put on a suit consisting of impermeable overalls, jacket and overshoes; that if a carpet were present this would be raised, rolled and placed in an impermeable bag for transportation to a steam disinfecting plant in the city. As in many localities such facilities are not available, the carpet is then so suspended that it can be sprayed on both sides with formalin solution, and later exposed to the action of formalin vapor used for disinfecting the chamber. It is also explained that the mattress and pillows would be simi-

larly treated. The drawers are removed and stood on edge and their contents, along with the bed clothing, suspended from a cord placed across the upper part of the chamber. Small openings are made in the mattress and a number of test objects introduced; one pillow is suspended from the cord and the other, as shown in the illustration, is laid on top of the mattress, with test objects interposed. Test objects are also placed upon the shelves and in the carriers. The carpet is then sprayed with formalin solution and it is explained to the class



A, formalin generator, heated by electricity; B, flat shelf for test objects; C, inclined shelf for fluid mediums; D and E, bed and chair of doll's chamber suit, the bureau of which can be seen in the back part of the cabinet; F, device for the introduction and removal of test objects, etc., this tray is withdrawn; G, same as F, but pushed into the cabinet; the leader from the letter G is on the conical plug that closes the opening through which the tray moves; H, test objects in tray F, outside the cabinet; I, test objects in tray G, inside the cabinet.

that the individual making the arrangements would now remove his impermeable suit and overshoes, step out of the room, close and lock the door, removing the knob and introducing the nozzle of the formalin generator. The method of sealing windows and doors is now explained and illustrated. Around some of the openings, or part of one door, cotton or rag strips are forced into position by the use of a case knife; other cracks around doors are closed by pasting over them

strips of paper or what is better but more likely to injure highly polished surfaces, strips of rubber adhesive plaster. The formalin generator is now started and the test begun. At appropriate intervals (2 to 10 minutes) a test object—either a pill box or an open petri dish—is removed from the carrier and given to the student who prepared the test object. In this way 50 students may be permitted to participate in the experiment and observe the results of disinfection over long or short periods. On the following day the cabinet is opened, any test objects in the interior are removed and portions of the carpet or other bodies permeable with difficulty, may be excised with sterile instruments and studied by cultural methods. It is possible to arrange on the carrier a container so that samples of the mixed air and gas can be removed from time to time for percentage determinations. It is unnecessary to describe other methods that may be tested as it is evident that any of the methods or appliances for disinfection of a room can be utilized and studied in similar ways; the apparatus readily yields itself to any method of fumigation.

The cabinet is also especially useful for the study of the insecticidal value of combined insecticides and disinfectants, or for the study of insecticides alone. Insects, such as mosquitos, bed-bugs, roaches, flies, and also small animals, if desirable, can be placed in the chamber, and the action upon them of known volumes of the gas can be investigated. Of course, the glass sides are impermeable, and the small strips of intervening wood offer practically no opportunity for the escape of gas; percentage leaks can be arranged for by valves; imperfect seals or the carrier can be left but partly closed. Flies and mosquitos lodge upon the glass, and can be watched with a lens if necessary, or they may be introduced in cages upon the test object carriers, and are therefore removable after selected periods. The chemic action of disinfecting agents can, in a small way, be studied by the use of this cabinet. Especially well does it afford an opportunity for observing the bleaching action of chlorin compounds; test paper saturated with dyes or special reagents may be suspended in the chamber to show clearly, by their reaction, the lines along which diffusion of evolved gas follows.

The apparatus has been in use in the laboratories of the Jefferson Medical College Hospital for a number of years, and has fulfilled our expectations. Where a number of men are moving about in a rather restricted space around the cabinet a formalin generator heated by oil or alcohol might be upset and constitute a danger that is avoided by the use of a generator heated by electricity as shown in the cut. The electric heated generators are not satisfactory for the disinfection of large quarters, as those with which I am familiar do not afford sufficient heat to secure rapid volatilization of the formaldehyd solution in large quantities.

*THE DISINFECTION OF CATHETERS BY
THE USE OF FORMALIN.*

BY RANDLE C. ROSENBERGER, M.D.

The following experiments were undertaken to determine the efficiency of formaldehyde in the disinfection of catheters.

The instruments used were of various sizes, ranging from No. 11 to No. 24. Some were of English web; others of soft rubber.

The apparatus to contain the catheters was an ordinary diploma case divided into a number of compartments by a removable, perforated, iron framework. Four instruments were in constant use in cases of cystitis, while three were practically new. The catheters from the cases of cystitis were, after simple washing in water, inoculated into bouillon. The new ones were boiled for five minutes, cooled rapidly by waving through the air, then infected with cultures of the *B. coli* and the *B. pyocyaneus*.

All the instruments were placed in the case, five cubic centimeters of formalin applied to absorbent cotton put in one end cap, and the case closed and kept at room temperature. No odor of formalin was detected at either end, or along the seams of the case.

After twenty-four hours the instruments were withdrawn, and inoculated into bouillon. It was found that those artificially infected showed no growth, while those from infected bladders mechanically cleansed still contained viable bacteria. (It might be mentioned that

from the catheters in constant use in cases of cystitis an organism resembling the colon bacillus was previously isolated.)

The instruments were enclosed for the second time, and for the same period. They were then taken out and inoculated into bouillon. The tubes were kept under observation for at least a week at ordinary room temperature, but no growths were noticeable.

The next experiments were to determine whether sterilized instruments were kept sterile by the reagent. To this end the catheters were all boiled for five minutes, inoculated into bouillon, and placed in the case. Formalin was applied as before, and the apparatus closed and again kept at room temperature.

In twenty-four hours the catheters were carefully removed from the case, inoculated into bouillon for the second time, and then replaced in the case. Two days later the instruments were dipped into culture media for the third time, thus making the exposure seventy-two hours. In none of the media inoculated was a bacterial growth evident, even after forty-eight hours' incubation at 37° C.

For the next experiments the instruments were boiled for one minute, infected with the *B. coli* and *B. pyocyaneus*, and dried for two hours in sterile Petri dishes in the incubator at 37° C. They were placed in the receptacle, five cubic centimeters of formalin applied as before, and the case sealed. Twenty-four hours later they were dipped into bouillon, carefully replaced in the case, and the latter again closed. No growths were noticed in any of the tubes of bouillon. After forty-eight hours inocu-

lations were made as before and the tubes of media incubated for forty-eight hours. No growths were noticeable in any of the tubes.

The instruments were next thoroughly washed of formalin, prepared as for the previous experiment, and instead of using formalin, three crushed pastilles of paraform were placed in the absorbent cotton, in the end cap as formalin was applied. The case was closed, and after twenty-four hours inoculations were made into bouillon, with the result that of six instruments infected three showed growths at ordinary room temperature. After seventy-two hours' exposure the bacteria were destroyed.

Another series of experiments were tried; using artificially infected instruments, drying them in sterile containers for eighteen hours in the incubator, placing them in the case, and exposing them to the action of formaldehyde generated from formalin (5 cubic centimeters). These exposures varied from thirty minutes to three hours, with the result that in all of the tubes of bouillon inoculated after these exposures bacterial growths were present. It will be seen that not even an inhibiting action was brought about by these short exposures.

Control cultures of all the bacteria were carried along, both at room temperature and in the incubator.

From these few experiments it can readily be seen that five cubic centimeters of formalin applied in the manner herein described will keep catheters sterile when exposed to this reagent for twenty-four hours.

The instruments, being boiled, can be placed in the case and kept there in-

definitely, as the gas does not injure the texture of the fabric. It has been proved by the writer and others that boiling the instruments for at least one minute, or as long as five minutes, renders them sterile.

Of the two substances—formalin and paraform—the former is to be preferred, as the latter does not generate the gas with sufficient rapidity without the application of heat.

Nancrede and Hutchings (*Journal of Michigan State Medical Society*, June, 1903) claim that formalin vapor will sterilize infected instruments in twenty-four hours, and that a shorter time has not as yet been determined. Mechanical cleansing from all dried pus, coagulated blood, or mucus will render sterilization easier and demand a shorter time to be effective.

CELLULOID STRIPS AND SHEETS FOR THE ORIENTATION OF GROSS PREPARATIONS, ESPECIALLY SPINAL CORDS, DURING FIXATION AND HANDLING, AND ALSO TO FACILITATE THE IDENTIFICATION OF PARTS REMOVED FOR MICROSCOPIC EXAMINATION.

By W. M. L. COPLIN, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

THESE strips consist of clear or gray celluloid, and measure 41 cm. in length, 4 cm. in breadth, and 0.3 cm. in thickness. The sides and ends are notched, the notches being 2 cm. apart; one face of the strip is roughened that it may be written upon with a lead-pencil. The removed cord attached to its membrane is secured in position on this strip by means of threads passing through the membrane and around the strip upon either side and the ends resting in the notches. If the cord be mounted a little to one side a free margin remains upon which figures may be placed identifying the parts to be studied, or parts removed for examination. The method recommended is that the upper end of the strip should be marked by a number, which in the note-book corresponds with the number of the cord or case; Roman numerals had best be used for this marking. If the numbers down the side of the strip are in Arabic, there should be no difficulty in keeping segments or blocks so that they readily may be identified and accurately placed.

The unroughened and unnotched strips cost \$1.50 per dozen. A janitor can roughen them in a few minutes with sand-paper; the notches are made with an ordinary triangular file.

2 COPLIN: CELLULOID STRIPS AND SHEETS FOR ORIENTATION

Strips of hard rubber, preferably red, may be used in the same way, but are more fragile. The roughened red rubber strips can be written upon with an ordinary pencil; such writing is read with difficulty on black rubber, but legends (ordinary labels) may readily be attached with celloidin or celluloid cement.

The plan just described may be applied to large masses or slabs of organs, as, for example, brain. In most instances thread cannot be used for attaching the specimen; when one surface is flat celloidin or gelatin (formalized) may be used.

The technique for attaching a slab of any tissue, for example, brain, is as follows:

The roughened surface of the celluloid sheet is cleaned and dried. The slab of tissue is removed from the fixative or other solution, rinsed in water and then in alcohol and quickly blotted dry. A sufficient quantity of thin celloidin is poured on the roughened and dry surface of the celluloid plate, and the slab of tissue, with the appropriate side upward, is pushed firmly into the still liquid celloidin and held in place for two to three minutes, by which time it is sufficiently adherent to be immersed in the preservative, which may be any of the fluids commonly used. The celluloid plate may be written upon with the ordinary graphite pencil and the positions of any blocks of tissue removed can be indicated by letters or numbers. The strips of celluloid may be used repeatedly, as any marks upon them can be erased. I have tried a number of inks for writing upon celluloid, but as yet have found none satisfactory.

Modifications and Improvements in the Petri-Dish-Plate-Glass-Gelatin Method of Mounting Glass Specimens.

By W. M. L. COPLIN, M.D.

(From the Laboratories of the Jefferson Medical College Hospital.)

C. J. PATTEN,¹ Professor of Anatomy, University College, Sheffield, suggests a method of mounting anatomic specimens for museum purposes, using a plaster-of-Paris slab, upon which permanent orientation is accomplished. Immediately after reading Prof. Patten's paper it occurred to me that the principle involved could be applied to the Petri-dish-plate-glass-gelatin method.² Dr. Funke was kind enough to make some preliminary experiments, which resulted in our adopting the following procedures:

The glass plate upon which the mount is to be made is thoroughly cleaned and a temporary receptacle made upon it by four strips of wood, 0.5 cm. in thickness, laid upon the surface in such a way as to form a rectangular well, 0.5 cm. in depth, the smallest transverse measurement of which exceeds by 0.5 cm. the diameter of the Petri dish to be used in the mount. The strips of wood, or, better, glass, are weighed or clamped in place. For the preparation of the plaster matrix the formula recommended by Prof. Patten has been adopted, except that we use what is called "dental" plaster of Paris; 27 ounces (approximately 830 gm.) are mixed with 22 ounces (approximately 680 c.c.) of water, this affording a mixture that sets smoothly and is of satisfactory consistency. Into the temporary vessel constructed on the surface of the plate glass the prepared plaster is poured, carefully

¹ British Medical Journal, November 19, 1904, p. 1378.

² Journal of the American Medical Association, August 13, 1904.

avoiding air-bubbles. While still soft the preparation to be mounted is removed from the final Kaiserling preservative, quickly blotted on a towel or filter paper, and gently bedded in the soft plaster. In order to rarify the contained air, the Petri dish is inverted, slightly warmed, and then pushed down over the specimen in the plaster until the margin of the dish rests firmly upon the plate glass. So soon as setting is complete the excess of plaster on the outside of the dish is removed, this part of the plate and dish cleaned, and the sealing completed with balsam. To prevent the growth of moulds on or around the specimen, it might be well to press into the plaster of Paris a crystal of thymol or possibly a small lump of camphor.

By the method just suggested the specimen is mounted in an air space unsurrounded by gelatin and containing no fluid. We have no preparations mounted sufficiently long to determine how well these will keep, but gelatin preparations similarly mounted have been preserved for more than a year. The method used by Littlejohn¹ is practically dry. The jars are closed with glaziers' putty. He strongly commends the method for toxicologic specimens, especially when the lesions result from carbolic acid or the mineral corrosive acids. The color preservation he regards as satisfactory, even after five or six years. At the last meeting of the American Medical Association, Dr. Wynn showed specimens preserved for months in Petri dishes which were not even sealed. If the foregoing methods are satisfactory, it is reasonable to assume that material will keep in the plaster-embedded condition.

As just described, but one surface of the specimen can be inspected, but it seems possible that the method could be so applied as to expose both sides of the specimen. In order to accomplish this, one surface of the mount should be fastened to the plate glass by means of formalized gelatin (gelatin containing 0.75 per cent. of formalin), and the

¹ Journal of Pathology and Bacteriology, 1903, vol. viii. p. 369.

walls of the temporary well for receiving the fluid plaster made of such a height that when filled to the necessary depth its contents will not overflow the enclosed specimen; the Petri dish is applied as already directed. So mounted both sides of the preparation could be inspected.

It also seems possible that these mounts could be made without the use of a Petri dish, but along this line of the inquiry we are unprepared to make any positive statements. A specimen of which it is desired that only one side should be exhibited could be cemented to the glass plate by means of formalized gelatin, and, as soon as the gelatin has set, liquid plaster poured over it should afford sufficient protection; the plaster might be rendered impervious by subsequent treatment with warm wax or oil, such as are used for painting on plaster.

The Petri-dish-gelatin mounts may be made more valuable if each preparation be accompanied by a section so placed that it can be subjected to microscopic examination. Every teacher knows how slides are prone to stray just when most wanted, and in order to avoid this difficulty the histologic preparation is made a part of the macroscopic mount. This is easily accomplished by fixing paraffin sections to a cover-glass by the albumin or other satisfactory method, removing the paraffin and subsequently treating the section exactly as though it were on a slide, except that the final mount is made near one corner of the glass plate instead of on a slide. In order to examine this mount a block just the height of the microscope stage is placed to one side and slightly in front, so as to share with the microscope stage the support of the plate glass.

THE PERMANENT PRESERVATION OF ANATOMIC, EMBRYOLOGIC, PATHOLOGIC AND BACTERIOLOGIC SPECIMENS.

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In teaching by modern laboratory methods, nothing is more important than the artistic and accurate preservation of material in such a manner as to retain permanently the natural colors and secure mounts that conveniently can be labelled, handled and exhibited. The old methods, yielding uncolored, bulky masses, possessing, save in form, little resemblance to the original, gave most unsatisfactory results, and hence museums more than five or ten years of age no longer meet the requirements of to-day. The specimens I exhibited at the Atlantic City Session of the Association received such flattering notice, and so many have written for the details of the method, that it seems desirable to publish in full the various steps necessary to attain the results shown. Except in minor details (which are essential), the method makes no claim to originality; it is the assembling of what seemed the best in several methods, published and unpublished, and still is replete with possibilities that have not been worked out. Undoubtedly the method could be applied to the preservation of botanic specimens, but having no facilities for experiment in this direction I have not attempted to adapt it to that purpose.

The method is based on the well-known Kaiserling process, and the permanent preservation in gelatin is but a modification of the old glycerin-jelly medium, long a standard agent with microscopists. Much of the detail requiring experiment has been worked out by Dr.

John Funke, to whose patience and care the beautiful results obtained are largely due. Petri dishes, mounted on glass plates, were first brought to my attention by Dr. S. W. Sappington, who used ground glass, which obscured one side of the specimen, but nevertheless yielded very beautiful results.

Dr. H. E. Radasch, associate in embryology in the Jefferson Medical College, has worked out the technic of attaching letters to the specimen so that the label may be made descriptive, like the legends in our text-books. My secretary experimented with various typewriter ribbons, and eventually found that the stock article called "The Record Ribbon" met all requirements.

THE FIXATION FLUID.

The agents used in the preliminary treatment of anatomic specimens are (1) the fixation fluid, (2) the developer, and (3) the final preservative, and for these purposes I have utilized the generally accepted fluids of the Kaiserling method. The fixation fluid is composed of

Formalin (any 40 per cent. aqueous solution of formaldehyd gas serves equally well)	250 c.c.
Potassium nitrate	10 gms.
Potassium acetate	30 gms.
Water	1,000 c.c.

The salts are dissolved in the water and the formalin is then added. It is desirable, but not strictly necessary, that the salts be chemically pure; a good commercial article gives satisfactory results, but many specimens of the salts contain iron, and even traces of this metal portend disaster. For this reason no metal is permitted to come in contact with the solution or the specimens during any stage of their preparation; the only exception to this rule has been the occasional use of lead for weighting down such organs as lungs and also lipomata and other tissues that tend to float, but even for this purpose pieces of tile, brick or crockery are better. The mixture is made in fifteen-gallon jars, with lips and lids of the form commercially used for the preservation of sauerkraut.

THE DEVELOPER AND THE PRESERVATIVE.

The developing fluid is alcohol. Most writers (including Kaiserling) recommend two strengths, an 80 per

cent. and a 95 per cent., but we use only the ordinary commercial article. So far as we can observe, methyl alcohol possesses no advantages.

The final preservative, in its liquid form, has the following formula:

Acetate of potassium.....	200 gms.
Glycerin	400 c.c.
Water	2,000 c.c.

The acetate and glycerin are thoroughly mixed and the water added. The order is probably of little importance in the preparation of either this or the fixation fluid, but in the latter one wishes to delay the addition of formalin as long as possible, as it is quite impracticable to stand over and stir the mixture after the formaldehyd is added. One word with regard to the water: Possibly distilled water is best, but some tap waters might be used; water from any mechanical filter using alum can not be trusted. Filtration of the fixation fluid is unnecessary; the preservative should be filtered through a thick pad of cotton placed at the bottom of a large funnel or percolator. As soon as the final fluid is prepared a lump of thymol (about 15 to 20 gms.), large enough to be seen and easily handled, is placed in the container, and each vessel of the final preservative should contain a piece of thymol sufficiently large to be picked out or left in the vessel when the fluid is poured out or used. When specimens are permanently preserved in this solution, a lump of thymol should be kept in the jar to prevent the growth of fungi.

THE GELATIN MEDIUM.

The solid medium in which the preparations are finally preserved is a 10 per cent. solution of gelatin in the acetate of potassium, glycerin and water mixture. This is prepared by soaking the requisite amount of gelatin in the mixture for 12 to 24 hours; the container is then placed on a water bath or in flowing hot water until the gelatin melts; this takes but a short time. The mixture is rendered decidedly acid to litmus by the addition of acetic acid, about 4 c.c. to the liter, and clarified by the use of egg albumin, exactly as in preparing gelatin media. Acetic acid favors complete coagulation of the albumin, tends to make the gelatin clearer, and, as originally suggested by Williams, acidity seems to assure better color preservation. The broken shells and whites of four eggs

should be used for each liter of the mixture. After filtration the prepared medium is bottled and placed on ice until solid, and then a large crystal of thymol is thrown on top of the solidified gelatin and the container stoppered. Prepared in this way, the medium keeps until needed. When wanted, the crystal of thymol is removed with forceps and the gelatin liquefied at a low temperature. The thymol should be taken out before warming the gelatin, otherwise it evinces a tendency to fragment, melts or is dissolved in such quantity that, when the fluid is cooled, a precipitate forms, rendering the medium grayish and slightly opaque. It is well known by bacteriologists that gelatins differ, and we have found at least one kind that can not be cleared satisfactorily. The preparation that has given us the best results is that known commercially as "W. H. No. 1,866." Some gelatins seem to contain a masked coloring which causes the finished preservative to appear decidedly red; it should be a light straw color and perfectly transparent. Care is necessary to exclude iron, and hence the gelatin should be made in glass beakers or porcelain vessels; new agate-ware free from cracks or shales may be employed, but it is so untrustworthy that time and patience are saved by avoiding it. I have not tried copper, but judge the excess of acetic acid would render its use risky.

THE SPECIMEN.

It is of the highest importance that the material to be preserved shall be received in a proper condition. Freshness is a prerequisite; when the blood has begun to yield its coloring matter and imbibition has tinged the specimen, only a motley result can follow. Our results with specimens that have been frozen or iced for any time, even if the colors at the beginning of the process seemed good, have not been satisfactory. Nothing shows this better than a pair of kidneys received fresh from an autopsy; one carried through immediately, and the other iced or kept in the refrigerator until the next day, when its preparation is begun; when obtained the organs may have appeared identical; after preparation the resemblance is superficial. The influence of blood imbibition (I use this term for combined hemolysis and hemoglobin diffusion as the hackneyed expression of the autopsy room) is such that a specimen left in a pan or on a plate containing a little blood-stained fluid will carry the

markings of the latter to the end. If fixation at once is not practicable, rinse off the blood stains and wrap the specimen in sufficient gauze, or a number of towels, to absorb any fluid that may escape; the fact that fluid escapes is proof that something is being lost, and it is attention to just such details that assures success.

THE ORIENTATION.

This is a most important step. The specimen is arranged, posed or oriented just as it is to appear when mounted; during fixation the stiffening action of the formalin gives a permanent shape even to such thin specimens as the intestine, and readjustment of such organs as the heart, lung, kidney or bladder becomes impossible. In this orientation every thread tied across the specimen will leave its mark, and each hole made will show; iron (tacks) can not be used, and even the slender entomologic pins leave small black holes; white thread (linen) is best; for pinning, wooden or quill toothpicks may be used. A number of cork blocks, 25 cm. square and 3.5 cm. thick, are especially useful for attaching and holding organs in position; intestine and other membranous specimens may be wound around such a block. The disadvantage of cork is the weight necessary to sink it, but even with this drawback it is better than glass. If both sides are to show, it is best to sew the specimen in a glass frame arranged for permanent mounting. If spread on cork or glass, four layers of thick, tough filter paper free from lint should be interposed between the specimen and the cork or glass. Cotton serves as well, but fixes tightly to albuminized surfaces; towels and cheesecloth are prone to mark the specimen with a screen effect. The cork, with the attached specimen turned downward, is thrown in the fixation fluid, and a brick placed on the top submerges the specimen and part of the cork. Care should be taken that the center of the specimen does not fall away from the cork; this can be prevented by obliquely placed toothpicks. Although highly recommended, we have not resorted to injection through the blood vessels, but for very large masses or the fixation of organs like the brain and liver it might be highly advantageous. Cysts, hydronephrotic kidneys, unopened intestine, stomach and other specimens containing cavities may be distended with the fixation fluid and sectioned later.

The formalin solution accomplishes more than one purpose. It fixes the specimen; I presume fixation is a coagulative process, at least in part, but it is more; the exact nature of the chemical change I shall not discuss at this time. The specimen stiffens, blanches, and becomes more or less friable and inelastic; the color changes appear to have ruined the mount. The fluid not only fixes, but also sterilizes the specimen, and, although surface color and contour may be preserved by surface fixation, penetration is necessary for satisfactory permanent preservation. For this reason a change to a second container of the fixation fluid is advised. The cork block or other retentive device is no longer needed, and in the second jar the specimens are packed lightly with towels or cotton at the bottom and interposed between. As soon as the first formalin solution becomes soiled it is thrown out, the second is moved back to become the first, the emptied container is washed and filled with fresh solution and replaces the second jar, now moved back to become the first. The solutions may be used repeatedly, provided specimens containing bile are excluded. Sometimes bile-stained specimens turn very green, all other colors being thereby obscured; such organs, usually livers, greatly discolor all the fluids into which they are placed. In preserving livers it is well to wash the bile from the gall bladder and rinse the surface of the organ thoroughly. I would advise, under all circumstances, that specimens of liver be carried through separately, as there is no way by which one can foretell how much bile-staining may result; sometimes no green tint develops, and beautiful color differentiations are obtained: we have no finer specimens than some of red atrophy put up over a year ago.

The most puzzling and unanswerable question, and at the same time an exceedingly important one, is how long must the formalin act? This depends entirely on the size and consistency of the specimen. A piece of stomach, intestine, diaphragm or other membrane will have fixed fully after three hours in each of the two formalin solutions. Half of a kidney should be left at least twelve hours in each solution, and a brain twenty-four hours in each solution. Prolonged immersion in the fixative solution may render development of the color impossible, but on the other hand under-fixation is sure to leave the blood coloring matter soluble, so that

it washes out or diffuses in the later handling. Large specimens, such as brains, livers, and even kidneys, if not sectioned when placed in the first solution should be freely incised, or, better, cut into slabs 4 to 8 cm. in thickness before entering the second fixing solution.

THE WASHING OUT.

The next step is getting rid of the excess of fixation fluid. This is accomplished by washing in running water for fifteen to twenty minutes, after which the specimen is transferred to the first alcohol. In my estimation the success of the process depends on the care and judgment exercised in the development of colors in the alcohol. The process should always begin in the morning, as I know of no safe criterion by which it is possible to foretell the length of time that will be necessary, and, as daylight is essential to watching the evolution of color, late afternoon and evening hours must be avoided. The excess of water is mopped off and the specimen completely submerged in commercial alcohol (94 per cent.); the color begins to appear in a few minutes, and as soon as it is fairly under way the tissue should be transferred to the second alcohol, and when restoration of color is complete the organ is quickly drained and submerged in the final preservative. When the restoration of color is complete fading begins, progresses rapidly, and, once the color is lost in alcohol, I know of no way by which its return can be secured; hence the process must be watched carefully. The stay in alcohols is also influenced by the future treatment to which the specimen is to be subjected. If it be a membrane, like a piece of intestine, even twenty minutes to a half hour for the two alcohols may be excessive; on the other hand, if it be a slab of an organ, the surface of which can be shaved down to the point where the alcohol has penetrated just to the proper degree, less care is necessary and over-development less likely to prove disastrous. As soon as the color is restored further action of the alcohol must be arrested by immersing the specimen in the first container of the potassium acetate, glycerin and water mixture, where it should be fully submerged and allowed to remain for the same length of time that it was in the alcohols, after which it is transferred to the second jar of the same fluid in which the preservation may be permanent, or after one or two

weeks, preferably sooner, the mount is completed in formalin-glycerin-gelatin. The first and second alcohols and the final preserving fluid are changed from time to time in the same way as already directed for changing the fixation fluid; sooner or later the first alcohol gives off strongly the odor of formalin, and the first preservative yields the odor of alcohol, when both should be changed. The method of changing suggested is the most economical, but probably is not so good as the complete renewal of all solutions; however, we have found the way advised efficient.

Specimens prepared as suggested preserve their color fairly well; to a large degree the permanency depends on the freshness of the material. Most observers lay great stress on the necessity of excluding light; probably darkness is better, but the chief difficulty lies in the macerating and solvent action of any solution, and to avoid these dangers a permanent solid medium is to be recommended, and for this purpose formalin-glycerin-gelatin is almost ideal.

FORMALIN-GLYCERIN-GELATIN MOUNTS IN PETRI DISHES.

The pieces of plate glass and Petri dishes used in preparing the mounts vary in size. The largest Petri dish that we have used is 20 cm. in diameter and requires a plate glass 9 by 11 inches. The following table gives the sizes of Petri dishes and glass plates necessary for all ordinary purposes; the conversion of the metric measurements to inches is approximate:

Petri Dishes.	Plate Glass.
20 cm.....	22.5x27.5 cm., 9x11 inches
15 cm.....	20.0x22.5 cm., 8x 9 inches
12 cm.....	20.0x22.5 cm., 8x 9 inches
10 cm.....	12.5x17.5 cm., 5x 7 inches
8 cm.....	12.5x17.5 cm., 5x 7 inches
6 cm.....	10.0x12.5 cm., 4x 5 inches
5 cm.....	7.5x10.0 cm., 3x 4 inches

The thickness of the plate glass is important, as thin pieces are often bent in handling, and any spring tends to loosen the attached dish. No matter what the surface dimensions, I am strongly convinced that the glass should not be less than one-fourth inch, and, better, three-eighths inch in thickness; a greater thickness might be desirable, but would add materially to the bulk and weight. The Petri dishes should be free from bubbles or rings, and when placed with the edge on plate glass should not rock, thus showing that the edge is true. The specimen to be mounted is placed in the dish, and this is

filled with final preservative for the purpose of ascertaining the quantity of gelatin that will be needed to complete the mount. We will say that this is found to be 100 c.c. Take 120 c.c. of the prepared gelatin, liquefied, and pour about one-half into the Petri dish, which must be thoroughly cleansed; place the specimen in this, carefully excluding air bubbles, and press it close to the bottom of the dish, using a light tile or glass weight if necessary. Even when every care is taken gelatin poured from one vessel to another tends to froth or form small bubbles which, after congelation, are difficult to remove; wherever such a bubble forms, it should be sucked up in a medicine dropper while the medium is still fluid. When properly oriented, dish and contained specimen are set aside in order to solidify the gelatin, using an iced chamber or the refrigerator, if the temperature of the room is too high. The mount may be left in this condition for several hours if desired, or mounting may be completed as soon as the gelatin is solid. Prolonged or too great cooling may cause corrugation of the surface, retraction from the sides of the dish, and permits less perfect fusion of the gelatin added later, and for these reasons is not recommended.

To complete the mount, pour on the solidified medium sufficient formalin to render the contained gelatin 0.75 per cent. formalin when the mount is completed. For example: If 100 c.c. of gelatin is necessary, 0.75 c.c. of formalin should be poured on the solidified layer. Fill the dish with the remainder of the gelatin, and place it on a piece of glass resting on the table in such a way that both can be picked up readily; while in this position put in place the glass plate that is to cover the Petri dish. As soon as the plate is in the desired position, grasp the mount between the two glass plates. turn it over quickly, and run a ring of gelatin around the junction between the plate and the dish. This is necessary because as the gelatin solidifies it contracts, and in the absence of an excess at the line of contact between plate and Petri dish, such contraction may permit the entrance of air. Set the dish aside for a few hours (over night or longer), until the gelatin is completely set. Run a knife around the Petri dish, holding it parallel with the side of the dish, thus cutting the gelatin loose from the side; the excess may readily be stripped off. Wash the plate quickly in cold water, dry rapidly, and

with a dropper run a thin band of gelatin containing 1 per cent. formalin around the line of contact between the Petri dish and the glass plate. This will quickly set, and in a day or so may be painted over with xylol balsam applied either with a brush or dropper; the first layer of balsam should be thin. As soon as the balsam ceases to be sticky to the finger, a second coat is applied, and this should be repeated until a sufficiently thick rim has been made. I have no doubt that a turn-table would be convenient for the application of the gelatin and balsam rings, but we have not found such an appliance necessary. It has been suggested that the initial gelatin ring

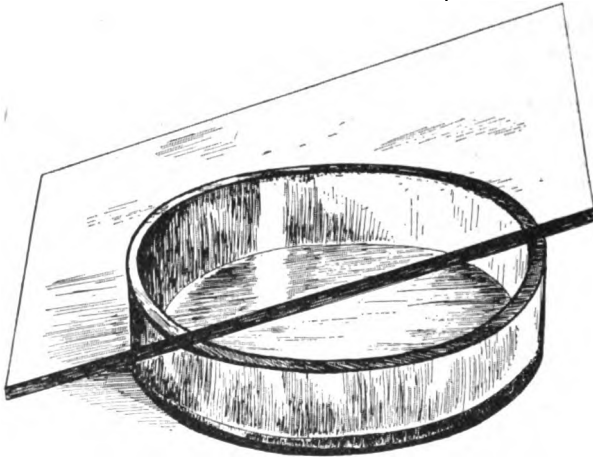


Fig. 1.—Method of applying the cover by tilting it over the dish. The specimen and contained gelatin are not shown in the illustration.

might be chromicised by the addition of bichromate of potassium, or by painting it over with a bichromate solution after it has solidified. A number of cements, including Bell's cement, asphaltum and gold-size, have been tried, but seem to possess no special advantages.

The most difficult part of the procedure is adjusting the glass plate on top of the Petri dish in such a way as to prevent the entrance of air at the time the mount is made. In the accompanying sketches (Figs. 1 and 2) an attempt is made to show how the plate cover is applied; one method is by tilting it in position, and the other by sliding it over the dish. By the latter method

a slight band of gelatin is kept ahead of the advancing plate, thereby preventing the entrance of air. Dr. Funke, who has been most successful in the preparation of these specimens, likes this method for the larger Petri dishes. During the experimental work necessary to perfect the process I was more successful with the other method. As neither is satisfactory under all conditions, some worker should be able to devise a means that is better than either. We have seriously considered submerging the dish either in gelatin or in water, but the methods detailed have been adequate. In the beginning there will be some difficulty in excluding air, but with a little experience one is able to secure satisfactory

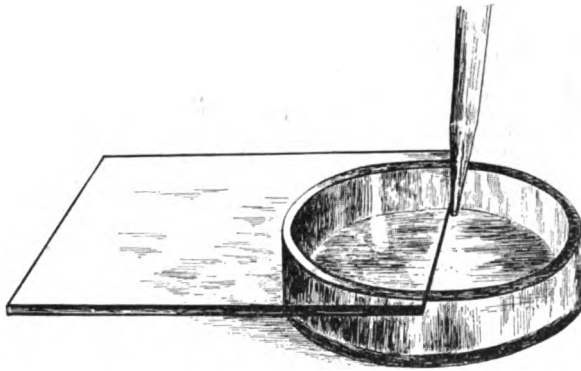


Fig. 2.—Sliding the glass plate into position. A. Medicine dropper by means of which a roll of fluid gelatin is kept in front of the advancing plate. This method is especially adapted to large mounts.

results. I do not know that a little air does any harm, although our experience has been that an air bubble invariably goes directly to the place where one does not desire it. Dr. Funke suggests that specimens having irregular and corrugated surfaces that afford numerous depressions in which air bubbles may lodge should be coated with gelatin before any attempt is made to mount them. Intestine frequently requires such treatment. He advises me also that lungs and other specimens containing spaces occupied by air be placed in a vacuum or chamber in which the air is rarefied in order that the gas in the interstices may more rapidly be displaced by the gelatin. We have not tried this method, but suggest it as a possible solution of the difficulty frequently

encountered in the preparation of lungs. The gelatin infiltration would be facilitated by immersing such specimens over night or longer in the medium kept liquid in the incubator.

Often a thin specimen would require so much of the medium to fill the dish that the resulting weight would make a cumbersome and unwieldy mount. This difficulty may be overcome by attaching the specimen to the dish by means of gelatin, and leaving the remaining space empty. This is best accomplished by flooding the surface of the glass plate with formalin-glycerin-gelatin; the specimen, for example a piece of intestine, is removed from the preserving liquid, lightly blotted with a towel and pressed into the gelatin, which quickly sets. The surface of the specimen to be viewed is left uncovered. As soon as the gelatin has set firmly, a slightly-warmed Petri dish is inverted over the specimen and pressed into the gelatin; the excess of gelatin outside the dish is removed with a knife or spatula; a narrow rim of gelatin painted around the junction between the Petri dish and the plate, and the seal completed by xylol balsam or other cement, as already directed. Sometimes such mounts loosen from the glass, but this difficulty has given us no trouble except in thick, weighty specimens, such as slabs of liver and bulky pieces of lungs. It could have been avoided by making thinner slices. We strongly advise this method for exhibiting the granular surface of a specimen where the unevenness would be obliterated by submersion in gelatin. It is recommended for exhibiting the granular surface of an incised lung in the red stage of croupous pneumonia, and for hemorrhagic infarcts. So far as we can see, the color preservation is fully as good as in submerged preparations. The method should be especially useful for the mounting of large brain sections, or slabs, for teaching purposes. If the Petri dish be shallow, so as to throw the specimen near the surface, an excellent view can be obtained. Mounting on the surface of gelatin is adapted to the exhibition of animal parasites that have been preserved by any of the formalin methods commonly used.

The principle can be applied to gelatin plates containing colonies. If the plates are in Petri dishes it is only necessary to invert the dish on the glass plate, ring it with gelatin and complete the seal as already directed.

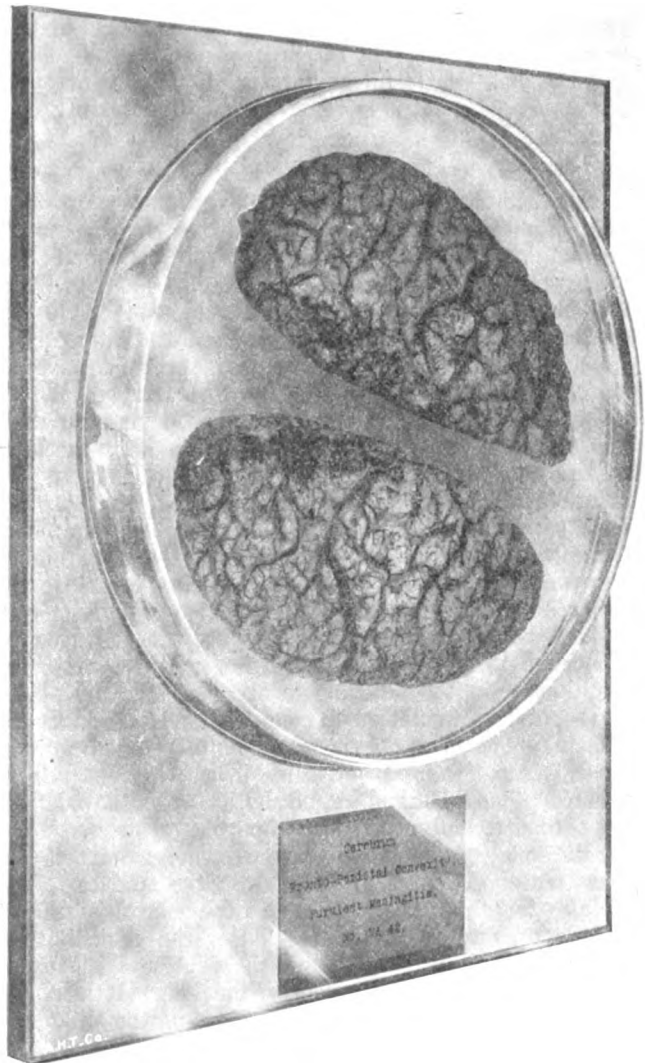


Fig. 3.—Completed mount in formalin-glycerin gelatin. All parts of the mount are well shown except the ring of cement joining the Petri dish to the glass plate; unfortunately the photograph has not brought out the transparent ring of balsam. The actual size of the glass plate is 22.5 cm. by 27.5 cm. (9 by 11 inches). The specimen is a part of the brain surface showing slight exudate and areas of hemorrhage, case of purulent meningitis.

If the old method of plating on glass, as originally advised by Koch, be used, the inverted Petri dish is warmed, a few drops of formalin placed on the gelatin, and the dish gently forced into position; the surrounding excess of gelatin is removed, and the sealing completed.

LABELLING.

The card used for labelling is the ordinary plain index card of medium thickness; on both sides the necessary legend is typewritten, using a "Record Ribbon"; the card is now trimmed so that at each edge it will be one-eighth inch narrower than the slide or other glass intended to cover it. The card is thrown into pure formalin and turned from side to side to prevent warping. While the card is soaking in the formalin (for which only a minute or so is necessary) a slide is cleaned by any of the approved methods. As a cover for the label we use a 2-inch by 3-inch slide, selecting, of course, the thinnest and most perfect with smooth edges. A 10 per cent. solution of gelatin, while still warm, is poured on the slide, the label is removed from the formalin, blotted between folds of filter paper, and quickly pressed down into the gelatin; a piece of filter paper is laid over it, and the label forced firmly against the slide, to which it adheres. As soon as the gelatin is set, which takes but a minute or so, the slide and its attached label are placed in the formalin solution to complete the fixation of the gelatin. The area on the glass plate selected for the label is now cleansed and some gelatin poured on the surface. The label and attached slide are removed from the formalin, blotted with filter paper and pressed down on the gelatin, the label, of course, going next to the glass plate. Weights are placed on the surface of the slide to force it into position, and the gelatin is allowed to pile up around the edges. After the gelatin is set firmly, a knife is run around the edge and the excess removed, as already described for the dish. A thin layer of gelatin is painted around the edges of the slide, and this, when dry, covered by xylol balsam in the same way as already directed for fastening Petri dishes in position. Where there is room for the label, it could be placed beside the specimen within the Petri dish; however, in that position it is more difficult to read and less readily seen when the mount is placed in a case. Dr. Radasch desired to label different parts of mounted em-

bryos in such a manner that students handling the preparations could identify certain structures. I had wished for the same thing and looked in vain for indestructible letters that could be used. Dr. Thomas C. Stellwagen, Jr., kindly made for me some amalgam letters that we attached to specimens, but the process was laborious and time-consuming. Dr. Radasch found a typewritten letter could be used; the paper containing the letter is trimmed to the desired size, immersed in formalin, removed, rapidly blotted, grasped in forceps and inserted in place while the imbedding gelatin is still fluid. He has many exquisite preparations lettered in this way, the labels constituting legends similar to those in our textbooks.

When completed, such specimens make artistic permanent mounts. (Fig. 3.) The gelatin lacks the macerating effect of fluids, and, so far as we can observe, preparations two years old are as fresh to-day as when first mounted. The mounts can be handled with wet hands; they may be washed with soap and water, and, as all parts are under glass, they are indestructible except by breaking. The fact that they are glass and appear much more fragile than they really are lead students to manifest care in handling them. Many of the preparations have been handled by hundreds of students and none has been broken. That they are not exceedingly fragile is indicated by our experience at Atlantic City. Nearly one hundred of these mounts were sent to the Session, and when the boxes were opened not one was found broken; two were dropped from the table, and one of these cracked, but was not withdrawn from the exhibit; few visitors noticed the break. In returning from Atlantic City three were broken, but the packing was not well done.

SPECIAL RECTANGULAR JAR.

While the gelatin method is especially adapted to mounts of membranes, tissues in thin slabs and relatively light preparations, there still remain a number of specimens that conveniently can not be prepared in this way. Over a year ago¹ I described a jar and adapted a clamp that, with some improvements, we are using to-day. This device (Fig. 4) consists of (1) a glass con-

1. Proceedings of the Pathological Society of Philadelphia, June, 1903.

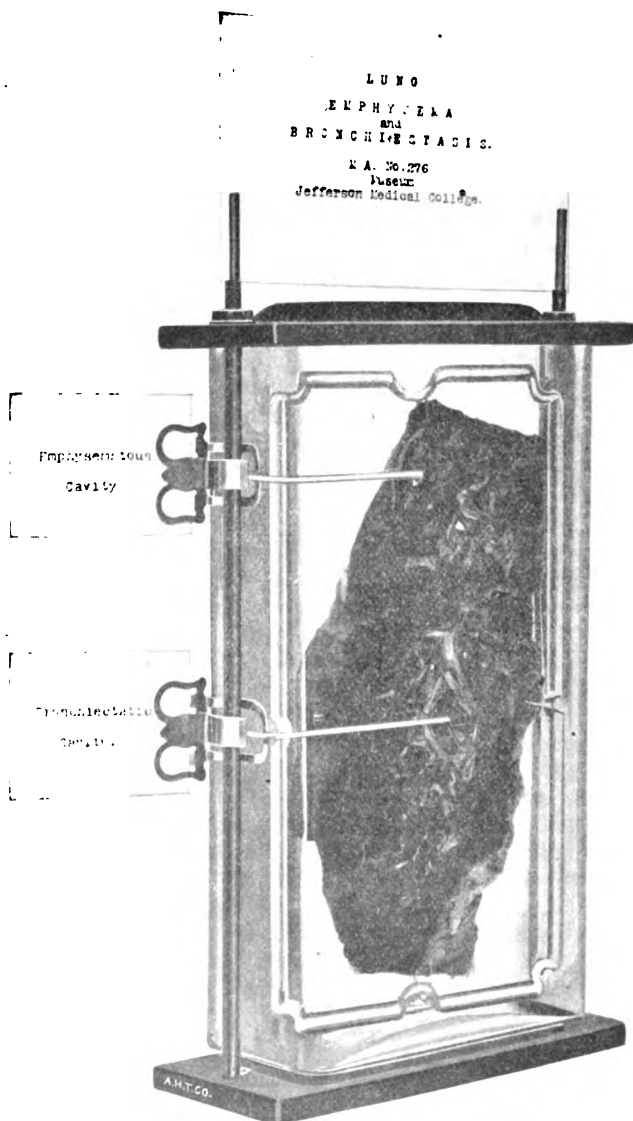


Fig. 4.—Improved rectangular jar, clamp and labelling device described in the text. The specimen photographed is a thin slab of lung showing emphysema and bronchiectasia. Contrary to the rule in such cases it is decidedly red, the high color being due to co-existing congestive condition resulting from associated cardiac lesions. This relatively bright red color has prevented accurate reproduction of the specimen. The labelling devices are well shown. In retouching the photograph the glass frame, by which the specimen is suspended, has been made unduly conspicuous, as there was no way by which we could determine how much detail would be lost in the reproduction; as a matter of fact, the frame is scarcely discernible when in position and covered by fluid. Reproduction five-twelfths natural size.

tainer, (2) a special metal clamp contrivance for securing a water-tight seal, and (3) includes two special labelling devices. The jar is 20 cm. high, 10 cm. wide and 4 cm. thick. When properly constructed the wall is practically the same thickness (0.4 cm.) at all points. Imported jars are recommended, as attempts to secure a jar of uniform thickness in this country have been unsuccessful. American manufacturers seem unable to make a jar that is not thinner at the corners, and therefore unadapted to our purposes. The clamp consists of two plates and two vertical rods which pass through the top and bottom plates, drawing these firmly to the jar by means of threads and nuts on the upper ends of the rods. The rods are split above the top plate for the reception of a label, which consists of an ordinary index card, on both sides of which the legend is written. The bottom of the jar is solid and rests on a rubber cushion; the top is closed by a similar rubber cushion that fits accurately into a recess that, in the figure, conceals it. These cushions are made of extra heavy, steam packing rubber that in cylinder heads of engines lasts for months. With the imported jar having thick sides the seal is perfect and in our mounts has remained so for over one year. If the jar be opened or the fluid changed often it may be necessary to renew these rubbers, which are comparatively inexpensive. Thin membranes, intestines and other specimens possessing too little rigidity to retain a permanent shape and position are attached to a frame made of glass rod.

A device that seems to me would be extremely advantageous in teaching is a labelled pointer than can be adjusted vertically on the rods at the side of the jar, and is used to indicate any particular point on the specimen to which it is desired to draw special attention. These pointers can be placed at any height, are easily shifted from place to place, readily transferable from jar to jar, and any number desired may be used on one specimen.

When properly sealed the jar may rest in any position, and of all devices for the preservation of specimens in a liquid medium it is most economical in space and fluid. It requires but 5 cm. (2 inches) shelf width and 13 cm. ($5\frac{1}{4}$ inches) base, so that seven jars without lateral cards can be placed on a shelf 6 cm. ($2\frac{1}{2}$ inches) wide and 88 cm. ($36\frac{1}{2}$ inches) in length. The amount of lateral space occupied by labels supported on pointers

depends, of course, on the size of the cards used for such labels. Even under unusual conditions such cards should not be over 5 cm. (2 inches) in length, and as but 4 cm. of this projects beyond the base of the jar, 17 cm. ($6\frac{3}{4}$ inches) will afford ample lateral space on the shelf, the depth of which remains the same as when side labels are not used. I have considered cases for these jars, and also for the gelatin mounted preparations, built on the principle used in the construction of sectional book-cases, and, should directors of museums find such jars acceptable, stacks could be arranged similar to those used in libraries where ready access to volumes is desirable.*

2. I am indebted to the Arthur H. Thomas Company of Philadelphia for the preparation of the illustrations that accompany this article.

LABORATORIES.

The following is a list of the formal Reports submitted, and Examinations made in the Laboratories of the Jefferson Medical College Hospital for the year ending December 31, 1904. The total is 3428; of these 405 are detailed written Reports, 2366 urinary examinations, 446 examinations of the blood, 114 of the sputum, 55 of the gastric contents, 13 of the feces and 29 for cytodagnosis of transudates, exudates, etc. The formal detailed Reports are numbered consecutively, beginning with the number following the last in the Report for the previous year, and bringing the total of these observations to nearly 3000. The Report closes with a table giving the number of examinations of various secretions, excretions, exudates, etc., the results having been submitted to the attending clinicians upon the usual blanks.

For the compilation of the table I am indebted to Dr. J. Howard Anderson, Resident Pathologist.

During the year Volume I of "Publications from the Laboratories of the Jefferson Medical College Hospital" has been issued. It contains 36 articles, embracing recent contributions to medical science by workers in the Laboratories, or articles based on Reports issued by the Department. The entire edition of the first volume has been distributed; Volume II is now in preparation and, it is hoped, may be issued during the present year.

The following is a list of specimens and materials examined in the Laboratories during the year 1904 :

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2561—Tissue from wound, for histologic diagnosis.	Tissue too dry to infiltrate.	2581—Inoculation from tibia, to determine character of infection.	Staphylococcus pyogenes albus.
2562—Inoculation from fluid from chest, to deter- mine character of in- fection.	Sterile.	2582—Tissue from rectum, for histologic diagnosis.	Villous papilloma of skin.
2563—Blood examination.	Polycythemia	2583—Tissue from larynx, for histologic diagnosis.	Tuberculous laryngitis.
2564—Water, for bacterio- logic examination.	Negative*	2584—Tissue for bacterio- logic examination.	Sterile.
2565—Water, for bacterio- logic examination.	Negative*	2585—Blood for Widal's test.	Negative*
2566—Water, for bacterio- logic examination.	Negative*	2586—Mamma and axillary glands for histologic diagnosis.	Encephaloid carcinoma.
2567—Water, for bacterio- logic examination.	Negative*	2587—Blood for Widal's test.	Positive. •
2568—Secretion from tumor of jaw, for bacterio- logic examination.	Staphylococcus pyogenes albus.	2588—Mamma and axillary glands, for histologic diagnosis.	Scirrhus carcinoma.
2569—Tumor from jaw, for histologic diagnosis.	Myxo-chondro- lymphangio-endo- thelioma.	2589—Urine.	Negative*
2570—Inoculation from rib, to determine character of infection.	Staphylococcus pyogenes aureus.	2590—Thyroid gland, for his- tologic diagnosis.	Hyperplastic goitre.
2571—Blood for Widal's test.	Positive.	2591—Urine.	Negative*
2572—Sac from abdomen, for histologic diagnosis.	Tuberculosis of peritoneum.	2592—Blood examination.	Polycythemia.
2573—Inoculation from kid- ney, to determine character of infection.	Sterile.	2593—Tissue from mamma and axilla, for histo- logic diagnosis.	Chronic produc- tive interstitial mastitis.
2574—Inoculation from re- tropharyngeal abscess, to determine character of infection.	Sterile.	2594—Tumor from thigh, for histologic diagnosis.	Infected sebaceous cyst.
2575—Inoculation from gall- bladder to determine character of infection.	Sterile.	2595—Tissue from mamma and axilla, for histo- logic diagnosis.	Scirrhus carcin- oma, ulcerating metastasis to lymph nodes.
2576—Tissue from tongue and sub-maxillary glands for histologic diagnosis.	Papilloma.	2596—Glands from axilla, for histologic diagnosis.	Carcinoma.
2577—Blood for Widal's test.	Positive.	2597—Tissue from neck, for histologic diagnosis.	Chondro-myo- melano-hemangio- endothelioma.
2578—Blood examination.	Polycythemia.	2598—Blood for Widal's test.	Positive.
2579—Mamma and axillary glands, for histologic diagnosis	Scirrhus carcin- oma; hyperplasia of lymph-nodes.	2599—Blood for Widal's test.	Negative*
2580—Inoculation from au- topsy, to determine character of infection.	Sterile.	2600—Blood, for bacterio- logic examination.	Pneumococcus.
		2601—Inoculation from ap- pendix, to determine character of infection.	Sterile.
		2602—(a) Mamma, (b) axillary glands for his- tologic diagnosis.	(a) Chronic case- ous tubercu- losis. (b) Hyperplasia.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2603—Inoculation from mamma, to determine character of infection.	Sterile.	2627—Section from sole of foot, for histologic diagnosis.	Melanotic tumor (?).
2604—Tumors from wrist and axilla, for histologic diagnosis.	Melanotic alveolar sarcoma.	2628—Tissue from prepatellar bursa, for histologic diagnosis.	Infected papilloma.
2605—Tissue from knee-joint, for histologic diagnosis.	Chronic tuberculosis.	2629—Blood examination.	Negative*
2606—Inoculation from wound, to determine character of infection.	Staphylococcus pyogenes aureus.	2630—Blood examination.	Negative*
2607—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	2631—Tumor from knee, for histologic diagnosis.	Osteo-chondroma.
2608—Portion of lower lip, for histologic diagnosis.	Squamous-cell epithelioma, metastasis to lymph-nodes.	2632—Tumors from (a) neck, (b) head, for histologic diagnosis.	(a) Lymphangio-endothelioma. (b) Pigmented cystic papillomata.
2609—Blood for Widal's test.	Positive.	2633—Fluid from knee-joint, for Bacillus typhosus.	Negative*
2610—Blood for Widal's test.	Positive.	2634—Blood for Widal's test.	Negative*
2611—Tissue from rectum, for histologic diagnosis.	Cylindric-cell epithelioma	2635—Discharge from hip, for bacteriologic examination.	Staphylococcus pyogenes albus and Bacillus mucosus capsulatus.
2612—Tissue from arm, for histologic diagnosis.	Granulating sinus.	2636—Inoculation from pleural effusion, to determine character of infection.	Sterile.
2613—Tumor from thigh, for histologic diagnosis.	Mixed-cell sarcoma.	2637—Tissue from larynx, for histologic diagnosis.	Round-cell sarcoma.
2614—Brain tumor, for histologic diagnosis.	Negative*	2638—Cyst, for histologic diagnosis.	Cystic goitre.
2615—Inoculation from leg, to determine character of infection.	Streptococcus pyogenes and Staphylococcus pyogenes aureus.	2639—(a) Lung, (b) liver, (c) kidney, (d) stomach, for histologic diagnosis.	(a) Emphysema and congestion with beginning pneumonia. (b) Cloudy swelling, congestion and intralobular cirrhosis. (c) Subacute diffuse nephritis. (d) Acute catarrhal gastritis; spheroidal-cell carcinoma of pylorus.
2616—Blood for Widal's test.	Positive.	2640—Inoculation from autopsy to determine character of infection.	Sterile.
2617—Blood for Widal's test.	Positive.	2641—Blood for bacteriologic examination.	Staphylococcus pyogenes albus.
2618—Blood for Widal's test.	Negative*	2642—Gastric contents.	Negative*
2619—Growth from finger, for histologic diagnosis.	Tissue received in a condition unfit for examination.	2643—Blood examination.	Negative*
2620—Blood for Widal's test.	Positive.	2644—Urine.	Albuminuria.
2621—Tumor from parotid region, for histologic diagnosis.	Ulcerating heman-gio-endothelioma of parotid gland.	2645—Inoculation from tonsils, to determine character of infection.	Streptococcus pyogenes and Staphylococcus pyogenes aureus.
2622—Amputated arm, for histologic diagnosis.	Chronic caseous tuberculosis of elbow.	2646—(a) Urine for hematuria, and hematoporphyrinuria; (b) blood examination.	(a) Negative*. (b) Hemolysis.
2623—Inoculation from arm, to determine character of infection.	Sterile.	2647—Blood for examination.	Polycythemia.
2624—Blood for Widal's test.	Positive.		
2625—Blood for Widal's test.	Positive.		
2626—Urine, for bacteriologic examination.	Bacillus tuberculosis		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2648—Blood for Widal's test.	Positive.	2673—Urine.	Albuminuria.
2649—Blood for Widal's test.	Positive.	2674—Blood for Widal's test.	Negative*
2650—Tumors from arm, for histologic diagnosis.	Melanotic alveolar sarcoma.	2675—Blood for Widal's test.	Positive.
2651—Urine.	Albuminuria.	2676—Blood examination.	Pernicious (?) anemia.
2652—Tumor from right wrist, for histologic diagnosis.	Lymphangioma.	2677—Tissue from neck, for histologic diagnosis.	Hyperplastic lymph-node.
2653—Blood for Widal's test.	Positive.	2678—Tissue from hip, for histologic diagnosis.	Mixed-cell sarcoma.
2654—Blood for Widal's test.	Positive.	2679—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
2655—Blood for Widal's test.	Positive.	2680—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.
2656—Sputum, for Bacillus tuberculosis.	Negative*	2681—Blood examination.	Negative*
2657—Blood examination.	Anemia.	2682—Blood for Widal's test.	Positive.
2658—Mamma, for histologic diagnosis.	Spheroidal-cell carcinoma.	2683—Blood for Widal's test.	Positive.
2659—Blood for Widal's test.	Positive.	2684—Blood for Widal's test.	Positive.
2660—Blood for Widal's test.	Negative*	2685—Inoculation from cyst contents, to determine character of infection.	Sterile.
2661—Inoculation from arm, to determine character of infection.	Streptococcus pyogenes.	2686—Tissue from bladder, to determine character of infection.	Myxosarcoma.
2662—Resected bowel, for histologic diagnosis.	Cylindric-cell epithelioma of sigmoid of colon.	2687—Tissue from angle of mouth, for histologic diagnosis.	Squamous-cell Epithelioma.
2663—Blood for Widal's test.	Positive.	2688—Blood for bacteriologic examination.	Bacillus coli communis.
2664—Blood for Widal's test.	Positive.	2689—Right mamma, for histologic diagnosis.	Fibrocystadenoma.
2665—Blood for Widal's test.	Positive.	2690—Blood for Widal's test.	Positive.
2666—Retroperitoneal tumor, for histologic diagnosis.	Lipoma.	2691—Blood for Widal's test.	Positive.
2667—Inoculation from heart to determine character of infection.	Negative*	2692—Blood for Widal's test.	Negative*
2668—Tumor from knee, for histologic diagnosis.	Osteo-chondroma.	2693—Tissue from thigh, for histologic diagnosis.	Inflammatory tissue.
2669—Omentum and pericolic fat, for histologic diagnosis.	Negative*	2694—Tissue from thigh, for histologic diagnosis.	Chronic indurating and caseating lymphadenitis.
2670—Tissue from sinus in neck, for histologic diagnosis.	Granulating tuberculous sinus, chronic caseous tuberculosis, pigimentary infiltration of lymph-nodes.	2695—Inoculation from teeth, to determine character of infection.	Streptococcus pyogenes and Staphylococcus pyogenes albus.
2671—Blood for Widal's test.	Positive.	2696—Blood for Widal's test.	Negative*
2672—Blood for Widal's test.	Negative*	2697—Blood for Widal's test.	Negative*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2698—Inoculation from autopsy, to determine character of infection.	Bacilli coli communis.	2719—Ovaries, for histologic diagnosis.	Chronic productive interstitial oophoritis; cystic degeneration.
2699—Tissue from (a) heart, (b) aorta, (c) lungs, (d) kidney, (e) intestine, for histologic diagnosis.	(a) Cloudy swelling; (b) atheroma; (c) congestion and edema with beginning pneumonia; (d) Chronic diffuse nephritis; (e) typhoid ulcers of ileum, ulcerative colitis, ischiorectal abscess.	2720—Blood for Widal's test.	Positive.
2700—Blood for Widal's test.	Positive.	2721—Blood for Widal's test.	Positive.
2701—Blood for Widal's test.	Negative*	2722—Uterine contents, for histologic diagnosis.	Endometritis; placental tissue.
2702—Inoculation from wound, to determine character of infection.	Staphylococcus pyogenes aureus.	2723—Intestine from rectosigmoid junction, for histologic diagnosis.	Catarrhal inflammation.
2703—Inoculation from urethra, to determine character of infection.	Sterile.	2724—Tissue from groin, for histologic diagnosis.	Squamous-cell epithelioma.
2704—Inoculation from urethra, to determine character of infection.	Sterile.	2725—Tissue from eye, for histologic diagnosis.	Papilloma.
2705—Blood for Widal's test.	Positive.	2726—Blood for Widal's test.	Negative*
2706—Tissue from liver, for histologic diagnosis.	Cloudy swelling; red atrophy; atrophic cirrhosis.	2727—Blood for Widal's test.	Positive.
2707—Bone from tibia, for histologic diagnosis.	Chronic suppurative osteomyelitis; granulating sinus.	2728—Blood for Widal's test.	Negative*
2708—Inoculation from tibia, to determine character of infection.	Bacillus pyocyaneus and Staphylococcus pyogenes aureus.	2729—Blood for Widal's test.	Positive.
2709—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	2730—Blood for Widal's test.	Positive.
2710—Inoculation from ascitic fluid, to determine character of infection.	Sterile.	2731—Tissue from uterus, for histologic diagnosis.	Placenta.
2711—Blood for Widal's test.	Positive.	2732—Water, for bacteriologic examination.	Negative*
2712—Blood for Widal's test.	Positive.	2733—Blood for Widal's test.	Negative*
2713—Blood for Widal's test.	Negative*	2734—Urine.	Bacillus coli communis.
2714—Inoculation from urethra, to determine character of infection.	Staphylococcus pyogenes albus.	2735—Feces, for bacteriologic examination.	Proteus vulgaris and Bacillus coli communis.
2715—Inoculation from (a) cervix; (b) urethra, to determine character of infection.	(a) Sterile. (b) Staphylococcus pyogenes albus.	2736—Blood for Widal's test.	Positive.
2716—Blood for Widal's test.	Positive.	2737—Blood for Widal's test.	Positive.
2717—Blood for Widal's test.	Positive.	2738—Blood for Widal's test.	Negative*
2718—Blood for Widal's test.	Negative*	2739—Blood examination.	Inflammatory leukocytosis.
		2740—Sub-maxillary glands, for histologic diagnosis.	Specimen Lost.
		2741—Blood examination.	Negative*
		2742—Blood for Widal's test.	Negative*
		2743—Blood for Widal's test.	Negative*
		2744—Blood for Widal's test.	Positive.
		2745—Blood for Widal's test.	Positive.

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2746—Tissue from uterus, for histologic diagnosis.	Uterine tissue showing glands.	2771—Blood for Widal's test.	Positive.
2747—Fecal matter, for in- testinal parasites.	Negative*	2772—Upper jaw and gland, for histologic diagnosis.	Lymphangio-endo- thelioma; hyper- plastic lymphadeni- tis.
2748—Fecal matter, for in- testinal parasites.	Negative*	2773—Blood for tumor cells.	Negative*
2749—Fecal matter, for in- testinal parasites.	Negative*	2774—Blood for Widal's test.	Negative*
2750—Urine.	Negative*	2775—Blood examination.	Anemia.
2751—Blood examination.	Leukocytosis.	2776—Intraligamentary cyst, for histologic diagnosis.	Papillary cyst-adenoma.
2752—Tissue from abdominal cavity, for histologic diagnosis.	Specimen lost.	2777—Pus from bowel, for bacteriologic examina- tion.	Bacillus coli communis.
2753—Tissue from right breast, for histologic diagnosis.	Specimen unfit for examination.	2778—Tissue from lower jaw, for histologic diagnosis.	Negative*
2754—Blood for Widal's test.	Positive.	2779—Blood for Widal's test.	Negative*
2755—Blood for Widal's test.	Positive.	2780—Tissue from rectum, for histologic diagnosis.	Columnar-cell epithelioma.
2756—Blood for Widal's test.	Positive.	2781—Inoculation from right knee, to determine character of infection.	Staphylococcus pyogenes aureus.
2757—Tissue from left mam- ma and axilla, for his- tologic diagnosis.	Specimen spoiled in preparation.	2782—Left mamma, for his- tologic diagnosis.	Fibrocystadenoma.
2758—Blood examination.	Leukocytosis; slight iodophilia.	2783—Thyroid gland, for histologic diagnosis.	Parenchymatous goitre.
2759—Growths from chest, for histologic diagnosis.	Spindle-cell sarcoma.	2784—Tissue from tongue, for histologic diagnosis.	Inflamed squam- ous-cell epithe- lioma.
2760—Uterus, tubes and ovaries for histologic diagnosis.	Specimen spoiled in preparation.	2785—Enucleated eyeball, for histologic diagnosis.	Vascular round- cell, melanosar- coma with accom- panying glaucoma.
2761—Pus from empyema, for bacteriologic diag- nosis.	Negative*	2786—Penis, for histologic diagnosis.	Inflammatory tissue.
2762—Masses from eyelids, for histologic diagnosis.	Round-cell and lympho-sarcoma.	2787—Blood for Widal's test.	Positive.
2763—Tissue from cervix, for histologic diagnosis.	Chronic endocer- vicitis with be- ginning cystic in- volution.	2788—Tissue from upper maxilla, for histologic diagnosis.	Ulcerating, mixed- cell fibrosarcoma.
2764—Blood examination.	Leukocytosis; slight iodophilia.	2789—Material from Steam- ship, for bacteriologic examination.	Fungi.
2765—Left mamma and axil- lary tissue, for histo- logic diagnosis.	Scirrhus carcinoma.	2790—Blood examination.	Leukocytosis.
2766—Sputum, for bacterio- logic examination.	Negative*	2791—Inoculation from jaw, to determine character of infection.	Sterile.
2767—Pus from breast abs- cess, for bacteriologic examination.	Pneumococcus and Staphylococcus pyogenes albus.	2792—Portions of cervical vertebrae and cord, for histologic diagnosis.	Compression and hemorrhage.
2768—Blood for Widal's test.	Negative*	2793—Mass from abdominal growth for histologic diagnosis.	Suppurative salpingitis.
2769—Tumor from abdomin- al wall, for histologic diagnosis.	Melanotic round- cell sarcoma.	2794—Blood for Widal's test.	Negative*
1770—Blood for tumor cells.	Present.	2795—Blood for tumor cells.	Negative*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2796—Blood for Widal's test.	Negative*	2822—Tissue from behind ear, for histologic diagnosis.	Melanotic heman-gio-endothelioma.
2797—Glands from neck, for histologic diagnosis.	Lymphosarcoma.	2823—Tissue from right mamma, for histologic diagnosis.	Chronic produc-tive mastitis.
2798—Blood for tumor cells.	Present.	2824—Tissue from epididy-mus, for histologic diagnosis.	Spermatic cyst.
2799—Blood for tumor cells.	Negative*	2825—Mamma for histologic diagnosis.	Scirrhus carcinoma.
2800—Tissue from right mamma, for histologic diagnosis.	Encephaloid carcinoma.	2826—Tissue from tongue, for histologic diagnosis.	Ulcerating, squam-ous-cell epithelioma
2801—Urine.	Albuminuria.	2827—Blood for Widal's test.	Positive.
2802—Blood for tumor cells.	Negative*	2828—Glands from sub-max-illary region for secondary malignant growth.	Negative*
2803—Tissue from jaw, for histologic diagnosis.	Connective tissue.	2829—Portion of tongue, for histologic diagnosis.	Squamous-cell epithelioma.
2804—Autopsy.	Aneurysm of in-nominate artery.	2830—Tissue from mouth, for histologic diagnosis.	Squamous-cell epi-thelioma of cheek.
2805—Blood for Widal's test.	Negative*	2831—Blood for Widal's test.	Negative*
2806—Testicle, for histologic diagnosis.	Syphilitic (?) orchitis.	2832—Growth from hand, for histologic diagnosis.	Papilloma.
2807—Blood for Widal's test.	Negative*	2833—Appendix, for histo-logic diagnosis.	Chronic catarrhal, chronic interstitial, acute diffuse, and acute catarrhal appendicitis.
2808—(a) Amputated leg, (b) femoral gland, for histologic diagnosis.	(a) Mixed-cell sarcoma of thigh. (b) Hyperplastic lymphadenitis.	2834—Tumor from upper jaw, for histologic diagnosis.	Giant-cell sarcoma of alveolar border.
2809—Pleural effusion, for bacteriologic examina-tion.	Tuberculous pleurisy.	2835—Tissue from cheek and gland, for histologic diagnosis.	Squamous-cell epithelioma.
2810—Blood examination.	Negative*	2836—Liver, for histologic diagnosis.	Melanotic alveolar sarcoma.
2811—Tissue from mamma, for histologic diagnosis.	Chronic mastitis and extensive cystic degeneration.	2837—Blood for Widal's test.	Negative*
2812—Urine.	Negative*	2838—Blood for Widal's test.	Positive.
2813—Inoculation from ap-pendix, to determine character of infection.	Bacillus coli communis.	2839—Spermatic cord, for histologic diagnosis.	Acute endarteritis, endophlebitis and chronic productive inflammation.
2814—Blood for Widal's test.	Positive.	2840—Blood for Widal's test.	Negative*
2815—Tissue from right tes-ticle for histologic diagnosis.	Gumma.	2841—Urethral stones, for diagnosis.	Calcium oxalate calculi.
2816—Tissue from ear, for histologic diagnosis.	Alveolar mixed-cell melanotic sarcoma.	2842—Blood for Widal's test.	Negative*
2817—Tissue from back, for histologic diagnosis.	Large round-cell sarcoma.	2843—Blood for Widal's test.	Negative*
2818—Tissue from right mamma, for histologic diagnosis.	Tuberculosis.	2844—Tissue from breast, for histologic diagnosis.	Chronic productive interstitial mastitis.
2819—Blood for Widal's test.	Negative*	2845—Nodules from intestine and peritoneum, for histologic diagnosis.	Chronic hyalofi-brous tuberculous peritonitis.
2820—Tissue from (a) uterus and (b) append-ages, for histologic diagnosis.	(a) Cylindric-cell epithelioma; fibro-ma and glandular endometritis. (b) papillary cyst-adenoma.		
2821—Blood for Widal's test.	Negative*		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2846—Drainage from gall-bladder, for bacteriologic examination.	Micrococci.	2871—Blood for Widal's test.	Positive.
2847—Sputum, for Bacillus tuberculosis.	Negative*	2872—Tumor from parotid region, for histologic diagnosis.	Endothelioma.
2848—Tissue from back, for histologic diagnosis.	Large round-cell melanotic sarcoma of skin.	2873—Tissue from right kidney, for histologic diagnosis.	Acute diffuse nephritis.
2849—Blood examination.	Negative*	2873—(a) Pancreas from autopsy, for histologic diagnosis.	Acute hemorrhagic pancreatitis; extensive fat necrosis; parapancreatic adiposa.
2850—Tissue from intestine, for histologic diagnosis.	Tuberculous peritonitis.	2874—Fluid from peritoneal cavity, for bacteriologic examination.	Sterile.
2851—Inoculation from peritoneal cavity, to determine character of infection.	Sterile.	2875—Inoculation and spreads from eye, to determine character of infection.	Xerosis bacillus.
2852—Growth from neck, for histologic diagnosis.	Melanotic mixed-cell sarcoma.	2876—Blood for Widal's test.	Positive.
2853—Inoculation from scalp, to determine character of infection.	Streptococcus pyogenes and Staphylococcus pyogenes aureus.	2877—Tumor from mamma, for histologic diagnosis.	Peri- and intracanalicular fibroma.
2854—Sputum, for Bacillus tuberculosis.	Negative*	2878—Mucous membrane from intestinal track, for histologic diagnosis.	Moderate catarrhal inflammation.
2855—Blood for Widal's test.	Negative*	2879—Tissue from appendix, for histologic diagnosis.	Fibroadenoma; chronic sclerosing and acute diffuse appendicitis.
2856—Urine for lead.	Present	2880—Tumor from neck, for histologic diagnosis.	Parenchymatous goitre.
2857—Blood examination.	Anemia.	2881—Tumor from neck, for histologic diagnosis.	Adenoma of thyroid.
2858—Bile, for bacteriologic examination.	Bacillus coli communis and Staphylococcus pyogenes aureus.	2882—Tissue from mamma, for histologic diagnosis.	Fibroadenoma.
2859—Blood for Widal's test.	Positive.	2883—Blood for Widal's test.	Negative*
2860—Tumor from nose, antrum and frontal sinus, for histologic diagnosis.	Small spindle-cell sarcoma.	2884—Blood for Widal's test.	Positive.
2861—Blood for Widal's test.	Positive.	2885—Bile from gall-bladder, for bacteriologic examination.	Sterile.
2862—Tumor from left mamma, for histologic diagnosis.	Intracanalicular fibroma.	2886—Parotid tumor and ramus of lower jaw, for histologic diagnosis.	Scirrhus carcinoma.
2863—Pleural effusion.	Cytologic study.	2887—Blood for Widal's test.	Negative*
2864—Tumor from left clavicle, and glands from right axilla, for histologic diagnosis.	Lymphosarcoma.	2888—Blood for Widal's test.	Negative*
2865—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	2889—Inoculation from cervical abscess, to determine character of infection.	Sterile.
2866—Urine, for bacteriologic examination.	Bacillus subtilis and Micrococcus ureæ.	2890—Tissue from cervical abscess, for histologic diagnosis.	Chronic caseous tuberculous lymphadenitis.
2867—Inoculation from abscess behind ear, to determine character of infection.	Bacillus pyocyaneus.	2891—Tissue from peritoneal cavity, for histologic diagnosis.	Organizing blood clot.
2868—Blood.	Cytologic study.		
2869—Blood.	Cytologic study.		
2870—Inoculation from ear, to determine character of infection.	Bacillus pyocyaneus.		

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2892—Fluid from peritoneal cavity.	Cytologic study.	2915—Inoculation from gall-bladder, to determine character of infection.	Sterile.
2893—Piece of ulnar nerve, for histologic diagnosis.	Chronic interstitial neuritis.	2916—Tissue from lips, for histologic diagnosis.	Macrocheilia.
2894—Tumor from orbital margin, for histologic diagnosis.	Dermoid cyst.	2917—Blood for Widal's test.	Positive.
2895—Pleural effusion.	Cytologic study.	2918—Tissue from (a) abdominal wall and uterus; (b) peritoneum; (c) lungs; (d) kidneys; (e) liver; (f) stomach and intestines; (g) brain and meninges, for histologic diagnosis.	(a) Suppurating wounds; (b) Acute suppurative peritonitis; (c) Congestion; (d) Cloudy swelling; (e) Cloudy swelling and focal necrosis; (f) Acute dilatation; (g) Edema.
2896—Pleural effusion for bacteriologic examination.	Negative*	2919—Blood for Widal's test.	Positive.
2897—Glands from neck, for histologic diagnosis.	Pseudo-leukemic lymphoma.	2920—Catgut, for bacteriologic examination.	Sterile.
2898—Inoculation from cerebrospinal fluid, to determine character of infection.	Pneumococcus.	2921—Blood for Widal's test.	Negative*
2899—Swabs from discharge from otitis media, for bacteriologic examination.	Staphylococcus pyogenes aureus.	2922—Blood for Widal's test.	Negative*
2900—Inoculation from appendix, to determine character of infection.	Bacillus coli communis.	2923—Tumor from buttock, for histologic diagnosis.	Mixed-cell fibrosarcoma.
2901—Inoculations and spreads from cervical canal, to determine character of infection.	Negative*	2924—Gland from groin, for histologic diagnosis.	Hyperplasia.
2902—Thyroid gland, for histologic diagnosis.	Parenchymatous goitre.	2925—Portion of left ileum, histologic diagnosis.	Erosion.
2903—Tissue from nose and cheek, for histologic diagnosis.	Lymphangio-endothelioma.	2926—Glands from axilla, for histologic diagnosis.	Hyperplastic lymphadenitis.
2904—Inoculation from axilla, to determine character of infection.	Sterile.	2927—Hand and part of forearm, for histologic diagnosis.	Ulcerating squamous-cell epithelioma.
2905—Tumor from chest wall, for histologic diagnosis.	Alveolar, small round-cell sarcoma	2928—Urine.	Nephritis.
2906—Blood for Widal's test.	Positive.	2929—Inoculation from (a) heart and (b) pericardium, to determine character of infection.	(a) Bacillus coli communis. (b) Sterile.
2907—Inoculation from autopsy, to determine character of infection.	Bacillus proteus vulgaris.	2930—Tissue from (a) lung. (b) intestine, for histologic diagnosis.	(a) Multiple hemorrhagic infarcts. (b) Hemorrhagic peritonitis, gangrene.
2908—Tissue from cheek, for histologic diagnosis.	Angioma.	2931—Right mamma, for histologic diagnosis.	Adenofibroma.
2909—Glands from neck, for histologic diagnosis.	Chronic caseous tuberculous lymphadenitis.	2932—Blood for Widal's test.	Positive.
2910—Urine.	Nephritis.	2933—Tissue from rectum, for histologic diagnosis.	Syphilis (?).
2911—Material from wrist and gland from forearm, for histologic diagnosis.	Giant-cell sarcoma.	2934—Tissue from leg, for histologic diagnosis.	Naevus pigmentosus.
2912—Inoculations from autopsy, to determine character of infection.	Sterile.	2935—Blood for Widal's test.	Positive.
2913—Gland and cyst wall from neck for histologic diagnosis.	Inflammatory tissue.	2936—Tissue from lips, for histologic diagnosis.	Lymphangioma.
2914—Blood for Widal's test.	Positive.	2937—Blood for Widal's test.	Negative*

MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.	MATERIAL EXAMINED AND OBJECT OF EXAMINATION.	RESULTS.
2938—Parotid gland and surrounding tissue for histologic diagnosis.	Squamous-cell epithelioma	2952—Tumor from hand, for histologic diagnosis.	Fibrochondroma.
2939—Tissue from thigh, for histologic diagnosis.	Naevus pigmentosus undergoing melanotic sarcomatous change.	2953—Blood for Widal's test.	Negative*
2940—Growth from leg, for histologic diagnosis.	Naevus pigmentosus, undergoing alveolar melanotic sarcomatous change.	2954—Water, for sewage contamination.	Negative*
2941—Urine.	Diabetes.	2955—Appendix, for histologic diagnosis.	Acute catarrhal and ulcerative appendicitis; infective lymphadenitis.
2942—Blood for Widal's test.	Negative*	2956—(a) Inoculation and spreads from appendix, (b) spread from lymph-node, to determine character of infection.	(a) <i>Bacillus coli communis</i> . (b) Sterile.
2943—Left mamma for histologic diagnosis.	Adenocarcinoma.	2957—Growth from alveolar process, for histologic diagnosis.	Giant-cell sarcoma.
2944—Placenta, for histologic diagnosis.	Obliterative endarteritis with multiple organizing infarcts.	2958—Sputum, for bacteriologic examination.	<i>Bacillus tuberculosis</i> , <i>pneumococcus</i> and <i>staphylococcus</i>
2945—Urine.	Nephritis.	2959—Placenta for histologic diagnosis.	Normal.
2946—Horny growth from scalp, for malignancy.	Negative*	2960—Blood for Widal's test.	Negative*
2947—Glands from neck, for histologic diagnosis.	Tuberculous adenitis.	2961—Blood for Widal's test.	Negative*
2948—Blood for Widal's test.	Positive.	2962—Blood for Widal's test.	Negative*
2949—Blood for Widal's test.	Negative*	2963—Water, for sewage contamination.	Negative*
2950—Fluid from knee joint, for bacteriologic examination.	Sterile.	2964—Tissue from autopsy, for histologic diagnosis.	Carcinoma.
2951—Feces, for <i>Bacillus tuberculosis</i> .	Present.	2965—Tumor from eyelid, for histologic diagnosis.	Examination not completed.

* The word "negative" is used in this report to mean: (1.) The material which the examination was conducted to demonstrate was not present. (2.) No information of diagnostic importance was obtained. Thus a blood or urinary examination yielding no diagnostic aid is marked "negative." The same word is used when, for example, the Widal test was applied without the occurrence of clumping. The different applications will be apparent.

For the following table, giving the number of examinations of urine, blood, sputum, gastric contents, feces and cytodiagnosis, I am indebted to Dr. J. Howard Anderson, Resident Pathologist.

REPORT OF URINE EXAMINATIONS.

(Not included in foregoing Report.)

Examiner.	No. of Examinations.	Examiner.	No. of Examinations.
Dr. Tomlinson	174	Dr. Porteous	373
Dr. Edwards	401	Dr. Chodoff	502
Dr. Stevenson	402	Dr. Callan	236
Dr. Kilgus	278		
		Total	2366

REPORT OF BLOOD EXAMINATIONS.

Examiner.	No. of Examinations.	Examiner.	No. of Examinations.
Dr. Tomlinson	38	Dr. Porteous	76
Dr. Edwards	73	Dr. Chodoff	107
Dr. Stevenson	84	Dr. Callan	26
Dr. Kilgus	42		
		Total	446

REPORT OF SPUTUM EXAMINATIONS.

Examiner.	No. of Examinations.	Examiner.	No. of Examinations.
Dr. Tomlinson	20	Dr. Porteous	19
Dr. Edwards	17	Dr. Chodoff	25
Dr. Stevenson	18	Dr. Callan	5
Dr. Kilgus	10		
		Total	114

REPORT OF EXAMINATIONS OF GASTRIC CONTENTS.

Examiner.	No. of Examinations.	Examiner.	No. of Examinations.
Dr. Tomlinson	8	Dr. Porteous	5
Dr. Edwards	7	Dr. Chodoff	13
Dr. Stevenson	6	Dr. Callan	6
Dr. Kilgus	10		
		Total	55

REPORT OF EXAMINATION OF FECES.

Examiner.	No. of Examinations.	Examiner.	No. of Examinations.
Dr. Tomlinson	2	Dr. Chodoff	6
Dr. Edwards	2	Dr. Callan	1
Dr. Kilgus	1		
Dr. Porteous	1	Total	13

CYTODIAGNOSES.

Examiner.	No. of Examinations.	Examiner.	No. of Examinations.
Dr. Tomlinson	3	Dr. Porteous	5
Dr. Edwards	5	Dr. Chodoff	4
Dr. Stevenson	7	Dr. Callan	2
Dr. Kilgus	3		
		Total	29

